```
=> fil reg; d ide
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STRUCTURE FILE UPDATES:   12 MAY 2005  HIGHEST RN 850400-93-0
DICTIONARY FILE UPDATES:  12 MAY 2005  HIGHEST RN 850400-93-0

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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

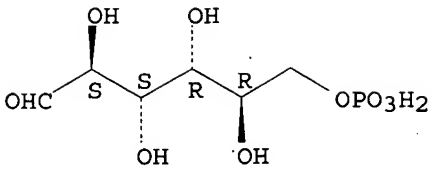
**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html


L40  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   3672-15-9  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   D-Mannose, 6-(dihydrogen phosphate) (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   D-Mannose, 6-phosphate (6CI)
CN   Mannose 6-phosphate (7CI)
CN   Mannose, 6-(dihydrogen phosphate), D- (8CI)
FS   STEREOSEARCH
DR   7683-50-3, 3311-11-3, 136309-77-8, 642477-31-4
MF   C6 H13 O9 P
CI   COM
LC   STN Files:   AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CEN, CSCHEM, EMBASE, MEDLINE,
       MSDS-OHS, PROMT, TOXCENTER, USPAT2, USPATFULL
         (*File contains numerically searchable property data)

Absolute stereochemistry.
```



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1051 REFERENCES IN FILE CA (1907 TO DATE)
51 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1052 REFERENCES IN FILE CAPLUS (1907 TO DATE)
23 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> □

=> fil reg; d stat que l5
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STRUCTURE FILE UPDATES: 12 MAY 2005 HIGHEST RN 850400-93-0
DICTIONARY FILE UPDATES: 12 MAY 2005 HIGHEST RN 850400-93-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

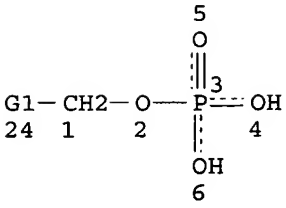
Please note that search-term pricing does apply when
conducting SmartSELECT searches.

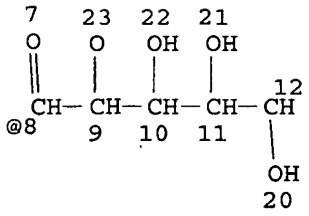
```
**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************
```

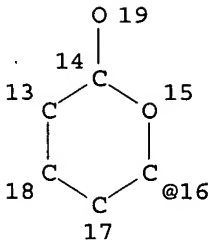
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

L3 STR







VAR G1=8/16
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
L5 738 SEA FILE=REGISTRY SSS FUL L3

100.0% PROCESSED 13930 ITERATIONS 738 ANSWERS
SEARCH TIME: 00.00.01

=> fil MEDLINE, CANCERLIT, JICST-EPLUS, AGRICOLA, PASCAL, BIOTECHNO, BIOSIS, CONFSCI, BIOTECHDS, DISSABS, TOXCENTER, EMBASE, WPIDS, ANABSTR

FILE 'MEDLINE' ENTERED AT 15:41:03 ON 13 MAY 2005

FILE 'CANCERLIT' ENTERED AT 15:41:03 ON 13 MAY 2005

FILE 'JICST-EPLUS' ENTERED AT 15:41:03 ON 13 MAY 2005
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FILE 'AGRICOLA' ENTERED AT 15:41:03 ON 13 MAY 2005

FILE 'PASCAL' ENTERED AT 15:41:03 ON 13 MAY 2005

FILE 'BIOTECHNO' ENTERED AT 15:41:03 ON 13 MAY 2005

FILE 'BIOSIS' ENTERED AT 15:41:03 ON 13 MAY 2005

FILE 'CONFSCI' ENTERED AT 15:41:03 ON 13 MAY 2005

FILE 'BIOTECHDS' ENTERED AT 15:41:03 ON 13 MAY 2005

FILE 'DISSABS' ENTERED AT 15:41:03 ON 13 MAY 2005

FILE 'TOXCENTER' ENTERED AT 15:41:03 ON 13 MAY 2005

FILE 'EMBASE' ENTERED AT 15:41:03 ON 13 MAY 2005

FILE 'WPIDS' ENTERED AT 15:41:03 ON 13 MAY 2005

FILE 'ANABSTR' ENTERED AT 15:41:03 ON 13 MAY 2005

=> d que nos l54; d que nos l55; d que nos l56; d que nos l63; d que nos l66

```
L6            2 SEA FILE=REGISTRY ABB=ON  9001-45-0 OR 9028-79-9 OR 9001-45-0
L7            4 SEA FILE=REGISTRY ABB=ON  9012-33-3 OR 37228-64-1 OR 37288-40-7
                  OR 9025-35-8
L8            1 SEA FILE=REGISTRY ABB=ON  9001-42-7
L40           1 SEA FILE=REGISTRY ABB=ON  3672-15-9
L41        2947 SEA L40
L42       19393 SEA (MANNOSE OR HEXOSE#)(3A) PHOSPH?
L43        1180 SEA M6P
L44      165346 SEA LYSOSOM?
L45       50085 SEA (L6 OR L7 OR L8)
L46      216724 SEA HEXOSAMINIDASE# OR GALACTOSIDASE# OR GLUCOCEREBROSIDASE#
                  OR ACETYLGLUCOSAMINIDASE# OR GLUCURONIDASE# OR GALACTOSE
                  OXIDASE#
L47          17 SEA HEXOS AMINIDASE# OR (GLUCOCEREBRO OR GLUCO CEREBRO)(W)
                  SIDASE# OR (ACETYLGLUCOS OR ACETYL GLUCOS)(W) AMINIDASE#
L48        2806 SEA ACETYL GLUCOSAMINIDASE#
L51        7944 SEA CARBONYL(3A) REACT?
L53         124 SEA MANNOPYRANOSYL#(3A) PHOSPH?
L54           3 SEA (L53 OR (L41 OR L42 OR L43)) AND (L44 OR L45 OR L46 OR L47
                  OR L48) AND L51
```

lysosomal enzymes

```
L6            2 SEA FILE=REGISTRY ABB=ON  9001-45-0 OR 9028-79-9 OR 9001-45-0
L7            4 SEA FILE=REGISTRY ABB=ON  9012-33-3 OR 37228-64-1 OR 37288-40-7
                  OR 9025-35-8
L8            1 SEA FILE=REGISTRY ABB=ON  9001-42-7
L40           1 SEA FILE=REGISTRY ABB=ON  3672-15-9
L41        2947 SEA L40
L42       19393 SEA (MANNOSE OR HEXOSE#)(3A) PHOSPH?
L43        1180 SEA M6P
L44      165346 SEA LYSOSOM?
L45       50085 SEA (L6 OR L7 OR L8)
L46      216724 SEA HEXOSAMINIDASE# OR GALACTOSIDASE# OR GLUCOCEREBROSIDASE#
                  OR ACETYLGLUCOSAMINIDASE# OR GLUCURONIDASE# OR GALACTOSE
                  OXIDASE#
L47          17 SEA HEXOS AMINIDASE# OR (GLUCOCEREBRO OR GLUCO CEREBRO)(W)
                  SIDASE# OR (ACETYLGLUCOS OR ACETYL GLUCOS)(W) AMINIDASE#
L48        2806 SEA ACETYL GLUCOSAMINIDASE#
L49     1900196 SEA COUPL?
L50      491056 SEA CONJUGAT?
L53         124 SEA MANNOPYRANOSYL#(3A) PHOSPH?
L55          20 SEA (L53 OR (L41 OR L42 OR L43)) AND (L44 OR L45 OR L46 OR L47
```

OR L48) (5A) (L49 OR L50)

```
L6            2 SEA FILE=REGISTRY ABB=ON  9001-45-0 OR 9028-79-9 OR 9001-45-0
L7            4 SEA FILE=REGISTRY ABB=ON  9012-33-3 OR 37228-64-1 OR 37288-40-7
                  OR 9025-35-8
L8            1 SEA FILE=REGISTRY ABB=ON  9001-42-7
L40           1 SEA FILE=REGISTRY ABB=ON  3672-15-9
L41        2947 SEA L40
L42       19393 SEA (MANNOSE OR HEXOSE#)(3A) PHOSPH?
L43        1180 SEA M6P
L44      165346 SEA LYSOSOM?
L45       50085 SEA (L6 OR L7 OR L8)
L46      216724 SEA HEXOSAMINIDASE# OR GALACTOSIDASE# OR GLUCOCEREBROSIDASE#
                  OR ACETYLGLUCOSAMINIDASE# OR GLUCURONIDASE# OR GALACTOSE
                  OXIDASE#
L47          17 SEA HEXOS AMINIDASE# OR (GLUCOCEREBRO OR GLUCO CEREBRO)(W)
                  SIDASE# OR (ACETYLGLUCOS OR ACETYL GLUCOS)(W) AMINIDASE#
L48        2806 SEA ACETYL GLUCOSAMINIDASE#
L49     1900196 SEA COUPL?
L50      491056 SEA CONJUGAT?
L53         124 SEA MANNOPYRANOSYL#(3A) PHOSPH?
L56          35 SEA (L53 OR (L41 OR L42 OR L43))(5A) (L49 OR L50) AND (L44 OR
                  L45 OR L46 OR L47 OR L48)
```

```
L6            2 SEA FILE=REGISTRY ABB=ON  9001-45-0 OR 9028-79-9 OR 9001-45-0
L7            4 SEA FILE=REGISTRY ABB=ON  9012-33-3 OR 37228-64-1 OR 37288-40-7
                  OR 9025-35-8
L8            1 SEA FILE=REGISTRY ABB=ON  9001-42-7
L40           1 SEA FILE=REGISTRY ABB=ON  3672-15-9
L45       50085 SEA (L6 OR L7 OR L8)
L49     1900196 SEA COUPL?
L50      491056 SEA CONJUGAT?
L63           8 SEA L40 AND L45 AND (L49 OR L50)
```

```
L42       19393 SEA (MANNOSE OR HEXOSE#)(3A) PHOSPH?
L43        1180 SEA M6P
L46      216724 SEA HEXOSAMINIDASE# OR GALACTOSIDASE# OR GLUCOCEREBROSIDASE#
                  OR ACETYLGLUCOSAMINIDASE# OR GLUCURONIDASE# OR GALACTOSE
                  OXIDASE#
L47          17 SEA HEXOS AMINIDASE# OR (GLUCOCEREBRO OR GLUCO CEREBRO)(W)
                  SIDASE# OR (ACETYLGLUCOS OR ACETYL GLUCOS)(W) AMINIDASE#
L48        2806 SEA ACETYL GLUCOSAMINIDASE#
L49     1900196 SEA COUPL?
L50      491056 SEA CONJUGAT?
L53         124 SEA MANNOPYRANOSYL#(3A) PHOSPH?
L60     4339526 SEA ENZYME#
L66          26 SEA (L42 OR L43 OR L53) (15A)((L46 OR L47 OR L48) OR L60)(15A)
                  (L49 OR L50)

=> s l54 or l55 or l56 or l63 or l66

L72          65 L54 OR L55 OR L56 OR L63 OR L66
```

```
=> fil capl; d que nos l11; d que nos l22; d que nos l23; d que nos l31; d que nos
l39

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FILE COVERS 1907 - 13 May 2005  VOL 142 ISS 21
FILE LAST UPDATED: 12 May 2005  (20050512/ED)

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  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE


L9              1 SEA FILE=REGISTRY ABB=ON  460740-37-8
L11             2 SEA FILE=CAPLUS ABB=ON  L9



L3                STR
L5              738 SEA FILE=REGISTRY SSS FUL L3
L6                2 SEA FILE=REGISTRY ABB=ON  9001-45-0 OR 9028-79-9 OR 9001-45-0
L7                4 SEA FILE=REGISTRY ABB=ON  9012-33-3 OR 37228-64-1 OR 37288-40-7
                    OR 9025-35-8
L8                1 SEA FILE=REGISTRY ABB=ON  9001-42-7
L12            6485 SEA FILE=CAPLUS ABB=ON  L5
L13           25022 SEA FILE=CAPLUS ABB=ON  (L6 OR L7 OR L8)
L14            8918 SEA FILE=CAPLUS ABB=ON  LYSOSOMAL/OBI
L15            4349 SEA FILE=CAPLUS ABB=ON  HEXOSES/CT
L16             584 SEA FILE=CAPLUS ABB=ON  HEXOSE PHOSPHATES/CT
L17             410 SEA FILE=CAPLUS ABB=ON  L15(L)PHOSPH?/OBI
L18            1280 SEA FILE=CAPLUS ABB=ON  MANNOSE 6 PHOSPHATE#/OBI OR M6P/OBI
L19          101961 SEA FILE=CAPLUS ABB=ON  CARBONYL#/OBI
L22               4 SEA FILE=CAPLUS ABB=ON  (L12 OR (L16 OR L17 OR L18)) AND (L13
                    OR L14) AND L19



L3                STR
L5              738 SEA FILE=REGISTRY SSS FUL L3
L6                2 SEA FILE=REGISTRY ABB=ON  9001-45-0 OR 9028-79-9 OR 9001-45-0
L7                4 SEA FILE=REGISTRY ABB=ON  9012-33-3 OR 37228-64-1 OR 37288-40-7
                    OR 9025-35-8
L8                1 SEA FILE=REGISTRY ABB=ON  9001-42-7
L12            6485 SEA FILE=CAPLUS ABB=ON  L5
```

```
L13        25022 SEA FILE=CAPLUS ABB=ON  (L6 OR L7 OR L8)
L14         8918 SEA FILE=CAPLUS ABB=ON  LYSOSOMAL/OBI
L20           39 SEA FILE=CAPLUS ABB=ON  L12 AND L13
L23            5 SEA FILE=CAPLUS ABB=ON  L20 AND L14


L3               STR
L5             738 SEA FILE=REGISTRY SSS FUL L3
L6               2 SEA FILE=REGISTRY ABB=ON  9001-45-0 OR 9028-79-9 OR 9001-45-0
L7               4 SEA FILE=REGISTRY ABB=ON  9012-33-3 OR 37228-64-1 OR 37288-40-7
                   OR 9025-35-8
L8               1 SEA FILE=REGISTRY ABB=ON  9001-42-7
L12           6485 SEA FILE=CAPLUS ABB=ON  L5
L13          25022 SEA FILE=CAPLUS ABB=ON  (L6 OR L7 OR L8)
L14           8918 SEA FILE=CAPLUS ABB=ON  LYSOSOMAL/OBI
L15           4349 SEA FILE=CAPLUS ABB=ON  HEXOSES/CT
L16            584 SEA FILE=CAPLUS ABB=ON  HEXOSE PHOSPHATES/CT
L17            410 SEA FILE=CAPLUS ABB=ON  L15(L)PHOSPH?/OBI
L18           1280 SEA FILE=CAPLUS ABB=ON  MANNOSE 6 PHOSPHATE#/OBI OR M6P/OBI
L21            327 SEA FILE=CAPLUS ABB=ON  (L12 OR (L16 OR L17 OR L18)) AND (L13
                   OR L14)
L27         325504 SEA FILE=CAPLUS ABB=ON  ?CARBONYL?/BI
L30          61515 SEA FILE=CAPLUS ABB=ON  L27(3A)REACT?/BI
L31              2 SEA FILE=CAPLUS ABB=ON  L21 AND L30


L3               STR
L5             738 SEA FILE=REGISTRY SSS FUL L3
L6               2 SEA FILE=REGISTRY ABB=ON  9001-45-0 OR 9028-79-9 OR 9001-45-0
L7               4 SEA FILE=REGISTRY ABB=ON  9012-33-3 OR 37228-64-1 OR 37288-40-7
                   OR 9025-35-8
L8               1 SEA FILE=REGISTRY ABB=ON  9001-42-7
L12           6485 SEA FILE=CAPLUS ABB=ON  L5
L13          25022 SEA FILE=CAPLUS ABB=ON  (L6 OR L7 OR L8)
L14           8918 SEA FILE=CAPLUS ABB=ON  LYSOSOMAL/OBI
L15           4349 SEA FILE=CAPLUS ABB=ON  HEXOSES/CT
L16            584 SEA FILE=CAPLUS ABB=ON  HEXOSE PHOSPHATES/CT
L17            410 SEA FILE=CAPLUS ABB=ON  L15(L)PHOSPH?/OBI
L18           1280 SEA FILE=CAPLUS ABB=ON  MANNOSE 6 PHOSPHATE#/OBI OR M6P/OBI
L24         280959 SEA FILE=CAPLUS ABB=ON  COUPL?/OBI
L25         106101 SEA FILE=CAPLUS ABB=ON  CONJUGAT?/OBI
L36          17655 SEA FILE=CAPLUS ABB=ON  LYSOSOME#/OBI
L37              9 SEA FILE=CAPLUS ABB=ON  (L12 OR (L16 OR L17 OR L18)) AND ((L13
                   OR L14) OR L36) (L) (L24 OR L25)
L38              9 SEA FILE=CAPLUS ABB=ON  (L12 OR (L16 OR L17 OR L18))(L)(L24 OR
                   L25) AND ((L13 OR L14) OR L36)
L39             12 SEA FILE=CAPLUS ABB=ON  L37 OR L38

=> s l11 or l22 or l23 or l31 or l39

L73             19 L11 OR L22 OR L23 OR L31 OR L39

=> dup rem l73,l72
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FILE 'CANCERLIT' ENTERED AT 15:41:26 ON 13 MAY 2005

FILE 'AGRICOLA' ENTERED AT 15:41:26 ON 13 MAY 2005

FILE 'PASCAL' ENTERED AT 15:41:26 ON 13 MAY 2005

FILE 'BIOTECHNO' ENTERED AT 15:41:26 ON 13 MAY 2005

FILE 'BIOSIS' ENTERED AT 15:41:26 ON 13 MAY 2005

FILE 'BIOTECHDS' ENTERED AT 15:41:26 ON 13 MAY 2005

FILE 'TOXCENTER' ENTERED AT 15:41:26 ON 13 MAY 2005

FILE 'EMBASE' ENTERED AT 15:41:26 ON 13 MAY 2005

FILE 'WPIDS' ENTERED AT 15:41:26 ON 13 MAY 2005

FILE 'ANABSTR' ENTERED AT 15:41:26 ON 13 MAY 2005

PROCESSING COMPLETED FOR L73
PROCESSING COMPLETED FOR L72
L74 41 DUP REM L73 L72 (43 DUPLICATES REMOVED)
ANSWERS '1-19' FROM FILE CAPLUS
ANSWERS '20-32' FROM FILE MEDLINE
ANSWER '33' FROM FILE AGRICOLA
ANSWERS '34-35' FROM FILE PASCAL
ANSWERS '36-37' FROM FILE BIOSIS
ANSWER '38' FROM FILE BIOTECHDS
ANSWER '39' FROM FILE EMBASE
ANSWER '40' FROM FILE WPIDS
ANSWER '41' FROM FILE ANABSTR

=> d ibib ed abs hitstr 1-19; d iall 20-41; fil hom

L74 ANSWER 1 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2005:238412 CAPLUS
DOCUMENT NUMBER: 142:291405
TITLE: **Coupling** of mannopyranosyl oligosaccharide containing **mannose-6-phosphate** (**M6P**) or other oligosaccharides bearing other terminal hexoses to **carbonyl** groups on oxidized **lysosomal** enzymes for treating **lysosomal** storage disease
INVENTOR(S): Zhu, Yunxiang
PATENT ASSIGNEE(S): Genzyme Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 33 pp., Cont.-in-part of U.S. Ser. No. 51,711.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005058634	A1	20050317	US 2004-943893		20040920
US 2002137125	A1	20020926	US 2002-51711		20020117
PRIORITY APPLN. INFO.:			US 2001-263078P	P	20010118
			US 2002-51711	A2	20020117

method of treat ment
method of making
Applicant

ED Entered STN: 18 Mar 2005

AB Methods to introduce highly phosphorylated mannopyranosyl oligosaccharide derivs. containing mannose-6-phosphate (M6P), or other oligosaccharides bearing other terminal hexoses, to carbonyl groups on oxidized glycans of glycoproteins while retaining their biol. activity are described. The methods are useful for modifying glycoproteins, including those produced by recombinant protein expression systems, to increase uptake by cell surface receptor-mediated mechanisms, thus improving their therapeutic efficacy in a variety of applications. Conjugation of phosphopentamannose-hydrazine to β-glucuronidase does not inactivate the enzyme. Chemical conjugating M6P-containing oligosaccharides onto recombinant human α-glucosidase (rhGAA) did not affect its enzymic activity. Conjugation of mono- and bis-phosphorylated oligomannose residues onto rhGAA improved its binding to CI-MPR (cation-independent mannose-6-phosphate receptor) and improved its uptake into cells in vitro. Modifying rhGAA with bis-M6P hydrazide resulted in a significant improvement in glycogen clearance in old and young pompe mice.

IT **9001-42-7 9001-45-0 9012-33-3,**
β-N-Acetyl-hexosaminidase **9025-35-8,** α Galactosidase A **37228-64-1,** β Glucocerebrosidase **37288-40-7,** α-N-Acetylglucosaminidase
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**coupling** of **mannose-6-phosphate** and other oligosaccharides to **lysosomal** enzymes for treating **lysosomal** storage disease)

RN 9001-42-7 CAPLUS
CN Glucosidase, α- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9001-45-0 CAPLUS
CN Glucuronidase, β- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9012-33-3 CAPLUS
CN Acetylhexosaminidase, β- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9025-35-8 CAPLUS
CN Galactosidase, α- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

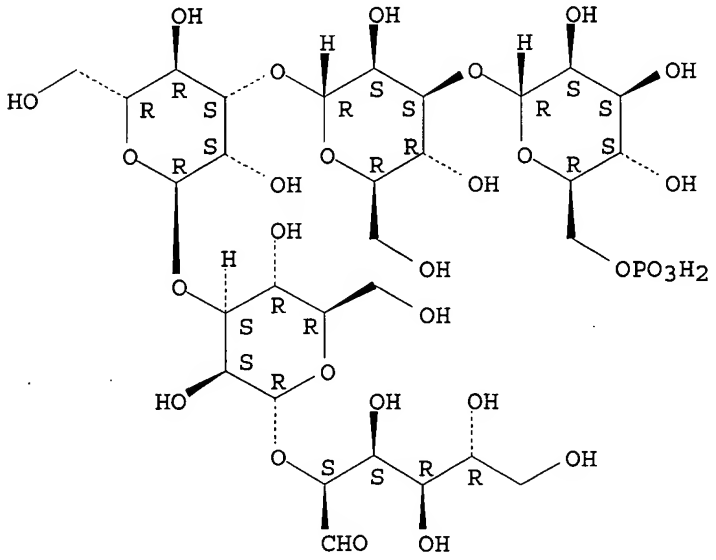
RN 37228-64-1 CAPLUS
CN Ceramidase, glucosyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 37288-40-7 CAPLUS
CN Acetylglucosaminidase, α- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **72672-17-4 460740-37-8 847937-81-9**, Bis-**M6p** Hydrazide
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**coupling** of **mannose-6-phosphate** and other oligosaccharides to **lysosomal** enzymes for treating **lysosomal** storage disease)
RN 72672-17-4 CAPLUS
CN D-Mannose, O-6-O-phosphono-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→2)- (9CI) (CA INDEX NAME)

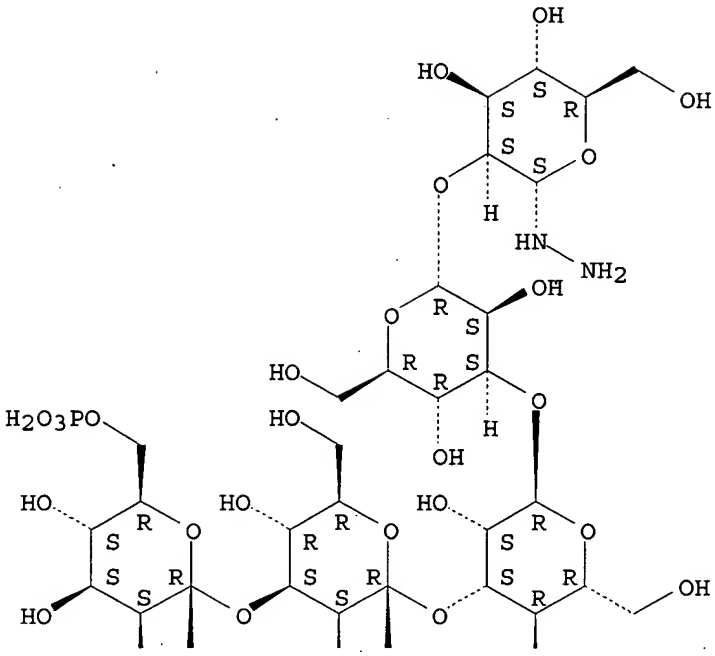
Absolute stereochemistry.



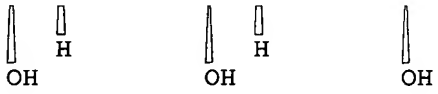
RN 460740-37-8 CAPLUS
CN α-D-Mannopyranose, O-6-O-phosphono-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→2)-1-deoxy-1-hydrazino- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



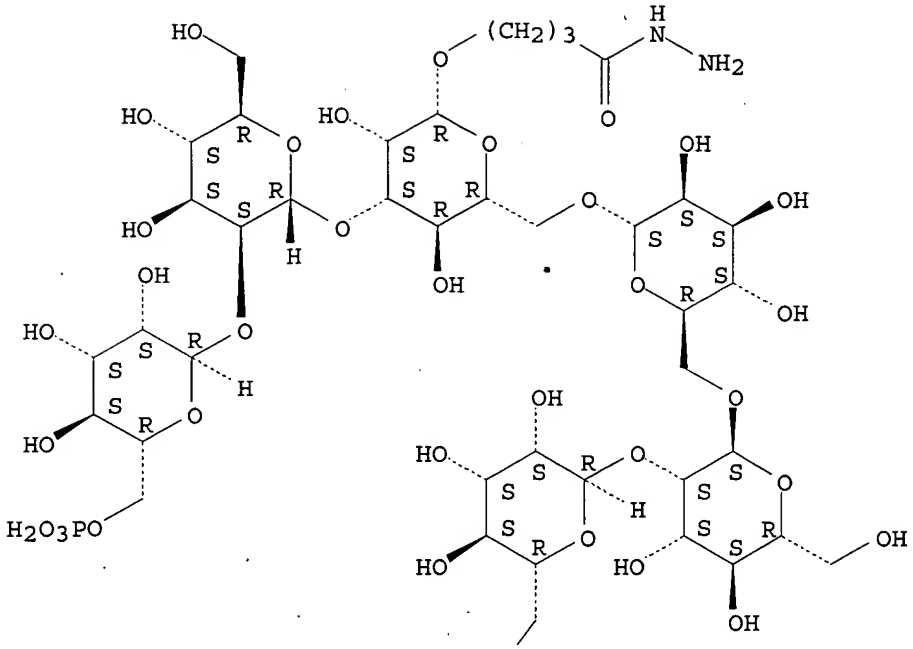
PAGE 2-A



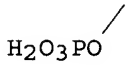
RN 847937-81-9 CAPLUS
CN Butanoic acid, 4-[(O-6-O-phosphono-α-D-mannopyranosyl-(1→2)-O-α-D-mannopyranosyl-(1→3)-O-[O-6-O-phosphono-α-D-mannopyranosyl-(1→2)-O-α-D-mannopyranosyl-(1→6)-α-D-mannopyranosyl-(1→6)]-β-D-mannopyranosyl)oxy]-, 1-hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



IT **9028-79-9**, Galactose oxidase
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(oxidation of **lysosomal** enzymes with; **coupling** of **mannose-6-phosphate** and other oligosaccharides to **lysosomal** enzymes for treating **lysosomal** storage disease)
RN 9028-79-9 CAPLUS
CN Oxidase, galactose (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L74 ANSWER 2 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:182383 CAPLUS
DOCUMENT NUMBER: 140:231203
TITLE: Methods for cell-free remodeling and glycoconjugation of glycopeptides, remodeling of α-galactosidase A peptides, and their therapeutic use for Fabry disease
INVENTOR(S): Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi
PATENT ASSIGNEE(S): Neose Technologies, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 761 pp., Cont.-in-part of Appl. No. PCT/US02/32263.

CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004043446	A1	20040304	US 2003-411037	20030409
WO 2003031464	A2	20030417	WO 2002-US32263	20021009
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GH, GM, GM, KE, KE, LS, LS, MW, MW, MZ, MZ, SD, SD, SL, SL, SZ, SZ, TZ, TZ, UG, UG, ZM, ZM, ZW, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ				
WO 2004099231	A2	20041118	WO 2004-US11494	20040409
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

US 2002-387292P	P	20020607
US 2002-391777P	P	20020625
US 2002-396594P	P	20020717
US 2002-404249P	P	20020816
US 2002-407527P	P	20020828
WO 2002-US32263	A2	20021009
US 2001-328523P	P	20011010
US 2001-344692P	P	20011019
US 2001-334233P	P	20011128
US 2001-334301P	P	20011128
US 2003-410897	A	20030409
US 2003-410913	A	20030409
US 2003-410930	A	20030409
US 2003-410945	A	20030409
US 2003-410962	A	20030409
US 2003-410980	A	20030409
US 2003-410997	A	20030409
US 2003-411012	A	20030409
US 2003-411026	A	20030409
US 2003-411037	A	20030409
US 2003-411043	A	20030409
US 2003-411044	A	20030409
US 2003-411049	A	20030409

ED Entered STN: 05 Mar 2004
AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. The

invention claims a method of remodeling an α-galactosidase A peptide in vitro by removing a saccharyl subunit from the peptide and contacting the truncated glycan with at least one glycosyltransferase and a glycosyl donor to transfer the glycosyl donor to the glycan moiety. The glycosyl donor may contain a modifying group such as a polymer, a therapeutic toxin, a detectable label, a reactive linker group, or a targeting mol. The invention specifically claims α-galactosidase glycopeptides containing mannooligosaccharide or sialyloligosaccharide structures and their modification with a galactosyltransferase, a sialyltransferase, or a mannosyltransferase and modified glycosyl donors such as UDP-Gal-polyethylene glycol (PEG)-transferrin , CMP-sialic acid linker-mannose-6-phosphate, CMP-sialic acid-PEG, or GDP-mannose-linker-ApoE. Conjugation of glycopeptides with PEG, for example, is intended to reduce the immunogenicity of peptides and prolong their half-life in circulation. Conjugation of glycopeptides with transferrin is intended to transport glycoconjugates across the blood-brain barrier. In addition, the invention claims therapeutic use of a glycoconjugated α-galactosidase A peptide for Fabry disease. Examples of the invention include synthesis of CMP-sialic acid, UDP-galactose, UDP-glucosamine, and UDP-galactosamine conjugates with polyethylene glycol, sialylation of recombinant glycoproteins antithrombin III, fetuin, and α1-antitrypsin by recombinant rat ST3Gal III, and glyco-remodeling of Cri-IgG1 monoclonal antibody. The general procedure for making UDP-GlcNAc-PEG is that the protected amino sugar diphospho-nucleotide is oxidized to form an aldehyde at the 6-position of the sugar. The aldehyde is converted to the corresponding primary amine by formation and reduction of the Schiff base. The resulting intermediate is contacted with the p-nitrophenol carbonate of m-PEG, which reacts with the amine, binding the m-PEG to the saccharide via an amide bond.

IT **9025-35-8**, α-Galactosidase A
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods for cell-free remodeling and glycoconjugation of glycopeptides, remodeling of α-galactosidase A peptides, and their therapeutic use for Fabry disease)
RN 9025-35-8 CAPLUS
CN Galactosidase, α- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L74 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:41094 CAPLUS
DOCUMENT NUMBER: 140:92570
TITLE: Induction of antigen-specific immunologic tolerance
INVENTOR(S): Kakkis, Emil D.; Lester, Thomas; Passage, Merry; Tanaka, Christopher; Yang, Rebecca
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. Pat. Appl. 2003 211,113.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004009906	A1	20040115	US 2003-429314	20030505
US 2003211113	A1	20031113	US 2002-141668	20020506
PRIORITY APPLN. INFO.:			US 2002-141668	A2 20020506

ED Entered STN: 18 Jan 2004

AB Antigen specific immune tolerance is induced in a mammalian host by administration of a toleragen in combination with a regimen of immunosuppression. The methods optionally include a preceding conditioning period, where immunosuppressive agents are administered in the absence of the toleragen. After the tolerizing regimen, the host is withdrawn from the suppressive agents, but is able to maintain specific immune tolerance to the immunogenic epitopes present on the toleragen. Optimally, the toleragen will have high uptake properties that allow uptake in vivo at low concns. in a wide variety of tolerizing cell types. In one example, the immune response to α-L-iduronidase is attenuated in a model of mucopolysaccharidosis.

IT **9001-42-7**, α-Glucosidase
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(administration of toleragen and immunosuppressive protocol for attenuation of immune response to)

RN 9001-42-7 CAPLUS

CN Glucosidase, α- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L74 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 2002:736789 CAPLUS
DOCUMENT NUMBER: 137:242146
TITLE: Methods for introducing **mannose 6-phosphate** and other oligosacharides onto glycoproteins
INVENTOR(S): Zhu, Yunxiang
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002137125	A1	20020926	US 2002-51711		20020117
US 2005058634	A1	20050317	US 2004-943893		20040920
PRIORITY APPLN. INFO.:			US 2001-263078P	P	20010118
			US 2002-51711	A2	20020117

OTHER SOURCE(S): MARPAT 137:242146

ED Entered STN: 27 Sep 2002

AB Methods to introduce highly phosphorylated mannopyranosyl oligosaccharide derivs. containing mannose 6-phosphate (M6P), or other oligosacharides bearing other terminal hexoses, to carbonyl groups on oxidized glycans of glycoproteins while retaining their biol. activity are described. The methods are useful for modifying glycoproteins, including those produced by recombinant protein expression systems, to increase uptake by cell surface receptor-mediated mechanisms, thus improving their therapeutic efficacy in a variety of applications. Thus, 6-O-phospho-pentamannose was reacted with hydrazine to form a 6-phosphopentamannosyl-hyrazine. This 6-phosphopentamannosyl-hyrazine was the reacted with an oxidized β-glucuronidase to form a phosphopentamannose-hydrazine derivatized β-glucuronidase that retained activity.

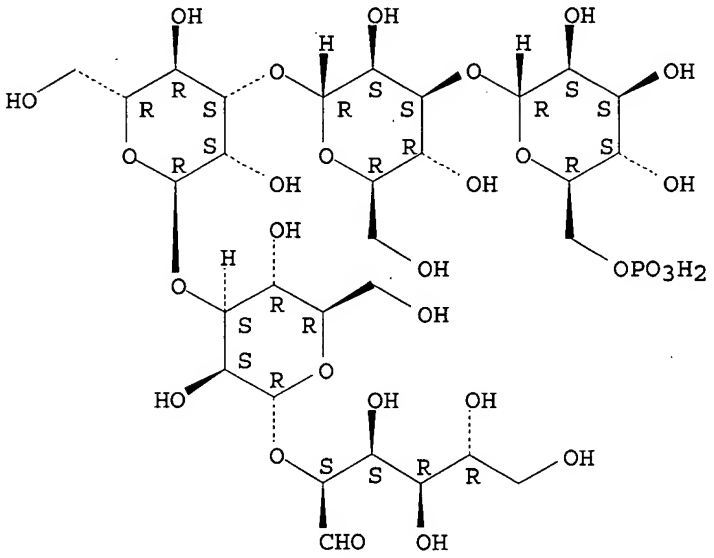
IT **9001-45-0**, β-Glucuronidase **9028-79-9**, Galactose oxidase **72672-17-4 359013-29-9 460740-36-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(methods for introducing **mannose 6-**

phosphate and other oligosacharides onto glycoproteins)
RN 9001-45-0 CAPLUS
CN Glucuronidase, β- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9028-79-9 CAPLUS
CN Oxidase, galactose (9CI) (CA INDEX NAME)

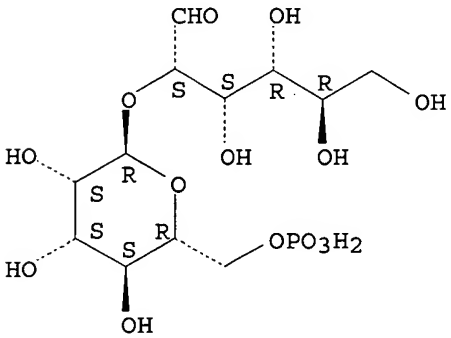
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 72672-17-4 CAPLUS
CN D-Mannose, O-6-O-phosphono-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→2)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 359013-29-9 CAPLUS
CN D-Mannose, 2-O-(6-O-phosphono-α-D-mannopyranosyl)- (9CI) (CA INDEX NAME)

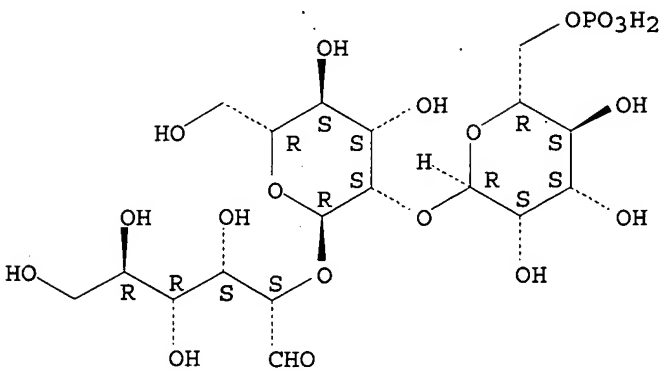
Absolute stereochemistry.



RN 460740-36-7 CAPLUS
CN D-Mannose, O-6-O-phosphono-α-D-mannopyranosyl-(1→2)-O-α-

D-mannopyranosyl-(1→2)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

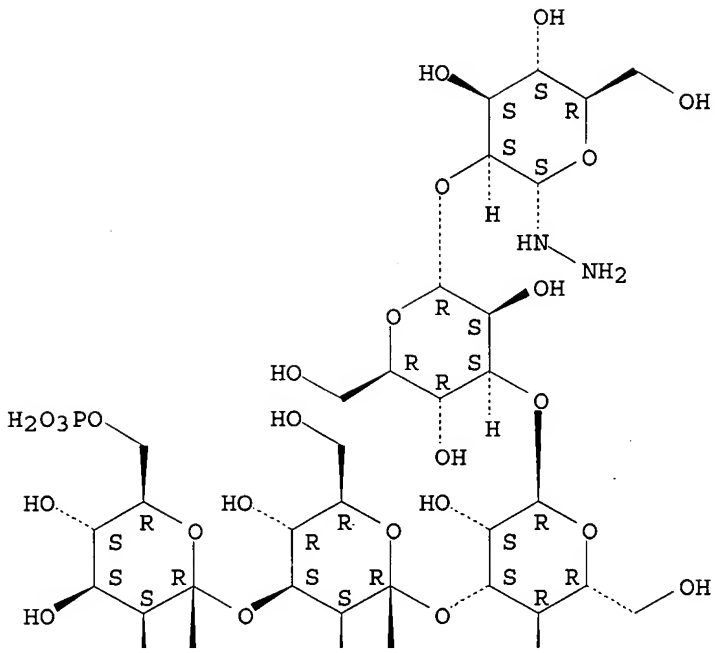


IT **9001-45-0DP**, β-Glucuronidase, **conjugated** with phosphopentamannosylhydrazine **460740-37-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(methods for introducing **mannose 6-phosphate** and other oligosacharides onto glycoproteins)
RN 9001-45-0 CAPLUS
CN Glucuronidase, β- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 460740-37-8 CAPLUS
CN α-D-Mannopyranose, O-6-O-phosphono-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→2)-1-deoxy-1-hydrazino- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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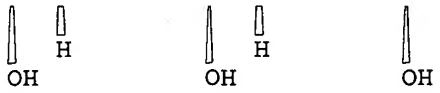


L74 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 12
ACCESSION NUMBER: 1990:586963 CAPLUS
DOCUMENT NUMBER: 113:186963
TITLE: Binding of **lysosomal** enzymes to the **mannose 6-phosphate** receptor: a novel binding assay that makes use of biotinylated receptor molecules, **coupled** to avidin-agarose
AUTHOR(S): Overdijk, Bernard; Van Steijn, G. J.
CORPORATE SOURCE: Dep. Med. Chem., Vrije Univ., Amsterdam, 1007 MC, Neth.
SOURCE: Journal of Receptor Research (1990), 10(1-2), 29-43
CODEN: JRERDM; ISSN: 0197-5110
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 23 Nov 1990
AB Binding assay procedures for receptor-ligand interactions should meet requirements such as ease of operation, reproducibility, and low costs. In the case of the mannose 6-phosphate receptor (MPR) for lysosomal enzymes, the earliest assay procedure made use of a crude membrane preparation containing MPR, that was sedimented after incubation with an enzyme solution The

bound enzyme activity was determined thereafter. With purification methods of MPE available, it was of interest to compare the binding of different lysosomal enzymes with these mol. MPR prepns. Therefore, a method was developed in which MPR was biotinylated, followed by coupling to avidin-agarose. Very small quantities of this gel (2 μL) appeared to be needed to bind sufficient amts. of lysosomal enzyme. The bound enzyme activity could be rapidly measured with high reproducibility, by incubating the agarose spheres directly with substrate solns. The binding properties of MPR, although biotinylated and immobilized, were not different from those obtained with crude MPR prepns. from rat liver membranes.

IT **9012-33-3**, β-Hexosaminidase
RL: ANT (Analyte); ANST (Analytical study)
(determination of, of **lysosomes**, immobilized mannose phosphate biotinylated receptor in binding assay for)

RN 9012-33-3 CAPLUS

CN Acetylhexosaminidase, β- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L74 ANSWER 6 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 19

ACCESSION NUMBER: 1980:529350 CAPLUS

DOCUMENT NUMBER: 93:129350

TITLE: p-Isothiocyanatophenyl 6-phospho-α-D-mannopyranoside **coupled** to albumin. A model compound recognized by the fibroblast **lysosomal** enzyme uptake system. 2. Biological properties

AUTHOR(S): Karson, Evelyn M.; Neufeld, Elizabeth F.; Sando, Gloria N.

CORPORATE SOURCE: Genet. Biochem. Branch, Natl. Inst. Arthritis, Metab. Dig. Dis., Bethesda, MD, 20205, USA

SOURCE: Biochemistry (1980), 19(16), 3856-60
CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 May 1984

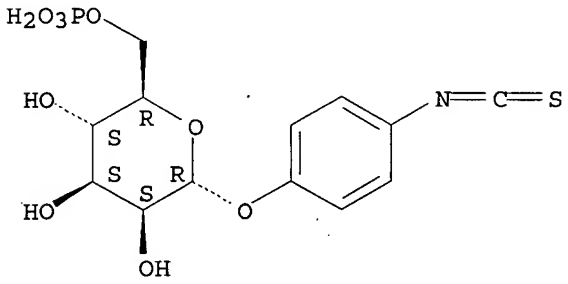
AB A conjugate of p-aminophenyl 6-phospho-α-D-mannopyranoside and bovine serum albumin interacted with the uptake system for lysosomal enzymes in cultured human diploid fibroblasts. Radioiodinated conjugate containing 20 mol of mannose 6-phosphate/mol of albumin was taken up by the cells and degraded to trichloroacetic acid-soluble fragments which were released into the medium. Unlabeled conjugate, mannose 6-phosphate, and a lysosomal enzyme, L-iduronidase, inhibited the uptake of the 125I-labeled conjugate (Ki = 2 + 10-8, 5 + 10-6, and 1.5 + 10-9M, resp.). Conversely, the uptake of L-iduronidase was competitively inhibited by the mannose 6-phosphate conjugate as well as by free mannose 6-phosphate; however, higher concns. of these compds. were required (Ki = 10-6 and 5 + 10-5M, resp.). Apparently although L-iduronidase and the conjugate are bound to the same receptor by mannose 6-phosphate residues, the uptake of the enzyme involves some addnl. structure that is not shared by the conjugate. Internalization of the radiolabeled mannose 6-phosphate-albumin conjugate was observed only in human diploid fibroblast strains. An SV40 transformed line of human fibroblasts as well as 3 permanent rodent fibroblast lines (CHO, NRK, and L cells) failed to take up the conjugate, presumably because they were deficient in receptors or in the ability to internalize receptor-conjugate complexes.

IT **74141-15-4D**, albumin **conjugates**
RL: PROC (Process)

Polysynthesis not Chemical Synthesis

(pinocytosis of, by fibroblast **lysosomal** enzyme uptake system)
RN 74141-15-4 CAPLUS
CN α-D-Mannopyranoside, 4-isothiocyanatophenyl, 6-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L74 ANSWER 7 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:182085 CAPLUS
DOCUMENT NUMBER: 142:254623
TITLE: Intrathecal administration of recombinant enzymes to treat lysosomal storage disorders
INVENTOR(S): Kakkis, Emil D.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 30 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005048047	A1	20050303	US 2003-651493	20030829
PRIORITY APPLN. INFO.:			US 2003-651493	20030829

ED Entered STN: 04 Mar 2005
AB The invention relates to the intrathecal administration of recombinant enzymes to treat lysosomal storage disorders. In an exemplary embodiment, intrathecal administration of human α-L-iduronidase (rhIDU) injections in mucopolysaccharidosis I (MPS I) affected animals resulted in significant enzyme uptake, significant rh-iduronidase activity in brain and meninges and a decrease of glycosaminoglycan (GAG) storage in cells of MPS I subjects to that of normal subjects. Intrathecal administration proved more effective than i.v. treatment at alleviating MPS I symptoms, indicating it is a useful method of treating lysosomal storage disorders.

L74 ANSWER 8 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:60754 CAPLUS
Correction of: 2004:1036571
DOCUMENT NUMBER: 142:233342
Correction of: 142:16836
TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S.

Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 42
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004241727	A1	20041202	US 2004-812731	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2004241727	A1	20041202	US 2004-812731	20040330
US 2004241727	A1	20041202	US 2004-812731	20040330
US 2004248169	A1	20041209	US 2004-812737	20040330
US 2004265869	A1	20041230	US 2004-812716	20040330
WO 2004112589	A2	20041229	WO 2004-US20836	20040621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
US 1999-115125P	P	19990106
US 2000-477148	B1	20000104
US 2002-268730	A2	20021009
US 2003-601518	A2	20030620
US 2004-802875	A2	20040312
US 2001-271955P	P	20010228
US 2001-275017P	P	20010312
US 2001-305340P	P	20010713
US 2002-85783	A2	20020228
US 2004-809675	A	20040325
US 2004-812731	A	20040330

ED Entered STN: 24 Jan 2005

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

IT **9012-33-3**, β-N-Acetylglucosaminidase
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(sequences of human schizophrenia-related genes and use for diagnosis, prognosis and therapy)

RN 9012-33-3 CAPLUS
CN Acetylhexosaminidase, β- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L74 ANSWER 9 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:97550 CAPLUS
DOCUMENT NUMBER: 138:164674
TITLE: Molecular markers for hepatocellular carcinoma and their use in diagnosis and therapy
INVENTOR(S): Debuschewitz, Sabine; Jobst, Juergen; Kaiser, Stephan
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003010336	A2	20030206	WO 2002-EP8305	20020725
WO 2003010336	A3	20041229		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10136273	A1	20030213	DE 2001-10136273	20010725
EP 1507871	A2	20050223	EP 2002-790191	20020725
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
WO 2004011945	A2	20040205	WO 2003-EP8243	20030725
WO 2004011945	A3	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1525477	A2	20050427	EP 2003-771105	20030725
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:

DE 2001-10136273	A	20010725
WO 2002-EP8305	W	20020725
WO 2003-EP8243	W	20030725

ED Entered STN: 07 Feb 2003
AB The invention relates to mol. markers occurring for hepatocellular carcinoma. The invention more particularly comprises gene sequences or peptides coded thereby which can be regulated upwards or downwards for hepatic cell carcinoma (HCC) in relation to healthy, normal liver cells in the expression thereof. The invention also relates to the use of said sequences in the diagnosis and/or therapy of HCC and for screening purposes in order to identify novel active ingredients for HCC. The invention also relates to an HCC specific cluster as a unique diagnostic

agent for HCC.

L74 ANSWER 10 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:928122 CAPLUS
DOCUMENT NUMBER: 138:12504
TITLE: Method for assaying biomolecules and other constituents using indicator conjugates with synthetic nucleounits in lateral flow, liquid, and dry chemistry techniques
INVENTOR(S): Smith, Jack V.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 46 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002182600	A1	20021205	US 2001-829563	20010411

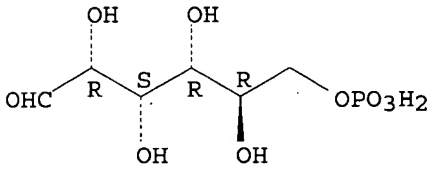
PRIORITY APPLN. INFO.: US 2001-829563 20010411
ED Entered STN: 06 Dec 2002
AB The present invention is a method for the use of particles made up of nucleotides or fragments of base groups of DNA and RNA mols. herein referred to as synthetic nucleounits which can be used as recognition mols. with specificity and sensitivity significantly greater than that of antibodies which are used in clin. diagnostics, biotechnol., and research. The method for detecting an analyte using nucleounits targeted to the analyte comprises (1) identifying a nucleounit from a mixture of synthetic random sequences of nucleounit libraries, (2) conjugating the nucleounit to an indicator for the analyte, and (3) detecting the analyte using the nucleounit-indicator conjugate in a buffer. Step 1 is carried out by (a) contacting the analyte with the mixture of synthetic random sequences of nucleounit libraries such that some nucleounits bind the analyte, (b) removing the unbound nucleounits by partitioning, and (c) amplifying the remaining nucleounits by PCR to obtain an enriched solution of nucleounits with high affinity for the analyte. Thus, a method and lateral flow test strip for detection of cytomegalovirus (CMV) presence in a biol. sample such as serum or urine is described. The strip is prepared with three solns., one containing anti-CMV antibodies, one containing "nucleounit to CMV antibody conjugated to red microparticles" and "red microparticles", and another containing "nucleounit to colored particles". The "nucleounit" may be an oligonucleotide aptamer specific for anti-CMV antibodies.
IT **9001-45-0**, Glucuronidase **9025-35-8**, α-Galactosidase
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(indicator; method for assaying biomols. and other constituents using indicator **conjugates** with synthetic nucleounits in lateral flow, liquid, and dry chemical techniques)
RN 9001-45-0 CAPLUS
CN Glucuronidase, β- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9025-35-8 CAPLUS
CN Galactosidase, α- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **56-73-5**, Glucose-6-phosphate

RL: ANT (Analyte); ANST (Analytical study)
(method for assaying biomols. and other constituents using indicator **conjugates** with synthetic nucleounits in lateral flow, liquid, and dry chemical techniques)
RN 56-73-5 CAPLUS
CN D-Glucose, 6-(dihydrogen phosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L74 ANSWER 11 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:359734 CAPLUS
DOCUMENT NUMBER: 131:2505
TITLE: Enzyme substrate delivery and product registration in one-step enzyme immunoassays
INVENTOR(S): Nelson, Alan M.; Pawlak, Jan W.; Pronovost, Allan D.
PATENT ASSIGNEE(S): Quidel Corporation, USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

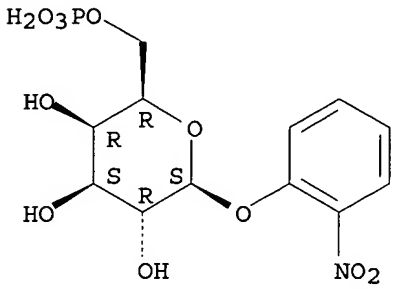
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9927364	A1	19990603	WO 1997-US23135	19971204
W: JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6306642	B1	20011023	US 1997-977183	19971124
US 2002025541	A1	20020228	US 2001-943031	20010829
US 6706539	B2	20040316		
US 2004152207	A1	20040805	US 2004-763466	20040122
PRIORITY APPLN. INFO.:			US 1997-977183 A	19971124
			US 2001-943031 A1	20010829

ED Entered STN: 11 Jun 1999
AB One-step enzyme immunoassays and apparatus are disclosed in which enzyme-antibody conjugate or label and enzyme substrate are separated until separation of bound and free enzyme conjugate or label is complete. This separation is accomplished by using variable flow paths, immobilization of substrate at the test line, placement of substrate in a sac or association with a particle label, enzyme product chemical capture, delay zone dissoln. and protected enzyme substrates. Enzyme substrate-loaded liposomes were prepared from cholesterol, distearoyl phosphatidylcholine, and distearoyl phosphatidylethanolamine-(p-maleimidophenyl)butyrate and conjugated with anti-human chorionic gonadotropin (hCG) monoclonal antibody derivatized with SPDP. In a lateral flow one-step enzyme immunoassay device, capture zone membranes contained anti-hCG antibody conjugated with phospholipase or complement C1q.
IT **20943-01-5**, o-Nitrophenyl-β-D-galactopyranoside-6-phosphate
225917-39-5

RL: ARG (Analytical reagent use); DEV (Device component use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(as enzyme substrate in hCG assay; enzyme substrate delivery and product registration in one-step enzyme immunoassays)

RN 20943-01-5 CAPLUS
CN β-D-Galactopyranoside, 2-nitrophenyl, 6-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

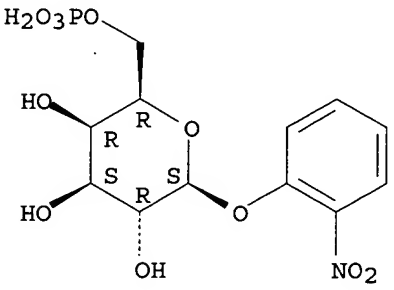


RN 225917-39-5 CAPLUS
CN β-D-Galactopyranoside, 2-nitrophenyl, 6-(dihydrogen phosphate), compd. with cyclohexanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

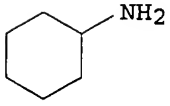
CRN 20943-01-5
CMF C12 H16 N O11 P

Absolute stereochemistry.



CM 2

CRN 108-91-8
CMF C6 H13 N



IT **9001-45-0D**, β-D-Glucuronidase, antibody **conjugates**

9025-35-8D, α-Galactosidase, antibody **conjugates**
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(enzyme substrate delivery and product registration in one-step enzyme immunoassays)
RN 9001-45-0 CAPLUS
CN Glucuronidase, β- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9025-35-8 CAPLUS
CN Galactosidase, α- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 12 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:352961 CAPLUS
DOCUMENT NUMBER: 129:37202
TITLE: Novel polymeric complexes for the transfection of nucleic acids, with residues causing the destabilization of cell membranes
INVENTOR(S): Midoux, Patrick; Monsigny, Michel
PATENT ASSIGNEE(S): I.D.M. Immuno-Designed Molecules, Fr.; Midoux, Patrick; Monsigny, Michel
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9822610	A1	19980528	WO 1997-FR2022	19971110
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2755976	A1	19980522	FR 1996-13990	19961115
FR 2755976	B1	19990115		
CA 2267833	AA	19980528	CA 1997-2267833	19971110
AU 9851239	A1	19980610	AU 1998-51239	19971110
AU 742818	B2	20020110		
EP 946744	A1	19991006	EP 1997-945903	19971110
EP 946744	B1	20040818		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001504344	T2	20010403	JP 1998-523257	19971110
AT 274066	E	20040915	AT 1997-945903	19971110
ES 2225992	T3	20050316	ES 1997-945903	19971110
US 6372499	B1	20020416	US 1999-297519	19990503

PRIORITY APPLN. INFO.: FR 1996-13990 A 19961115
WO 1997-FR2022 W 19971110

OTHER SOURCE(S): MARPAT 129:37202
ED Entered STN: 11 Jun 1998

AB The invention concerns a complex between at least a (neg. charged) nucleic acid and at least a pos. charged polymeric conjugate, the bond between the nucleic acid and the polymeric conjugate being electrostatic in nature, the polymeric conjugate containing a polymer formed by monomer units bearing free NH3+ functions, and being such that: the free NH3+ functions of said monomer units are substituted in a ratio of ≥10 % by residues causing in weak acid medium destabilization of cell membranes, in particular the endocytosis vesicle membrane, and/or endosomes; said residues having further the following properties: they comprise a functional group for being fixed to said polymer, they are not active as recognition signal identified by a cell membrane receptor, they can comprise at least one free NH3+ function; said uncharged residues having further the following properties: they comprise at least a hydroxyl group, they are not active as recognition signal identified by a cell membrane receptor, the hydroxyl groups of said uncharged residues being capable of being substituted by at least a mol. which constitutes a recognition signal identified by a cell membrane receptor, with reservation that the whole set of free NH3+ functions is at least 30 % of the number of monomer units of the polymeric network of said polymeric conjugate.

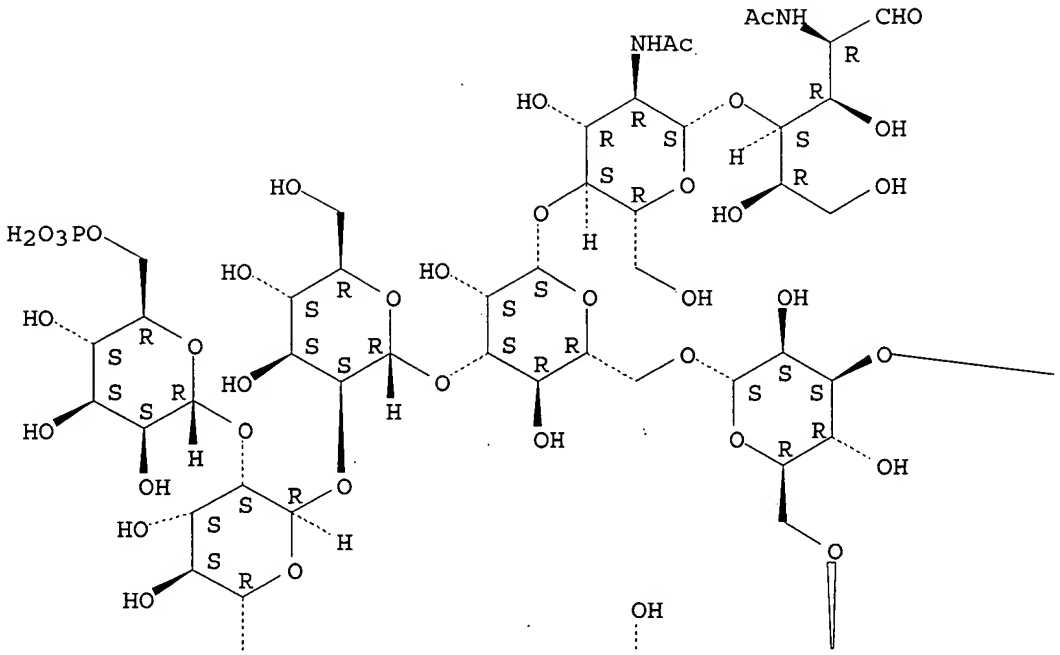
IT **208337-46-6 208342-24-9**
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(polymeric complexes for the transfection of nucleic acids, with residues causing the destabilization of cell membranes)

RN 208337-46-6 CAPLUS

CN D-Glucose, O-α-D-mannopyranosyl-(1→3)-O-[O-6-O-phosphono-α-D-mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→6)]-O-α-D-mannopyranosyl-(1→6)-O-[O-6-O-phosphono-α-D-mannopyranosyl-(1→2)-O-α-D-mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→3)]-O-β-D-mannopyranosyl-(1→4)-O-2-(acetylamino)-2-deoxy-β-D-glucopyranosyl-(1→4)-2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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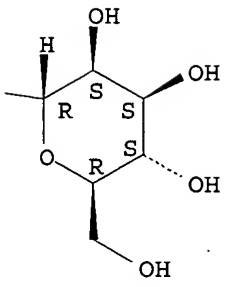

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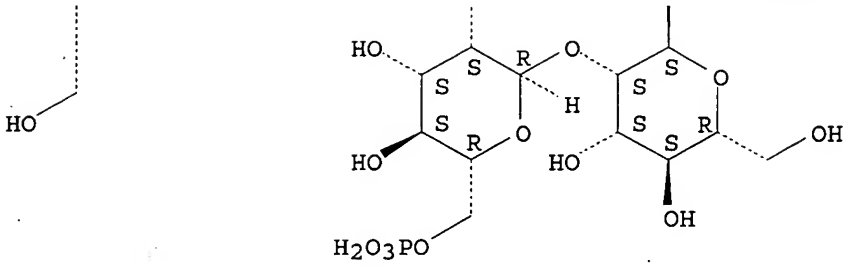
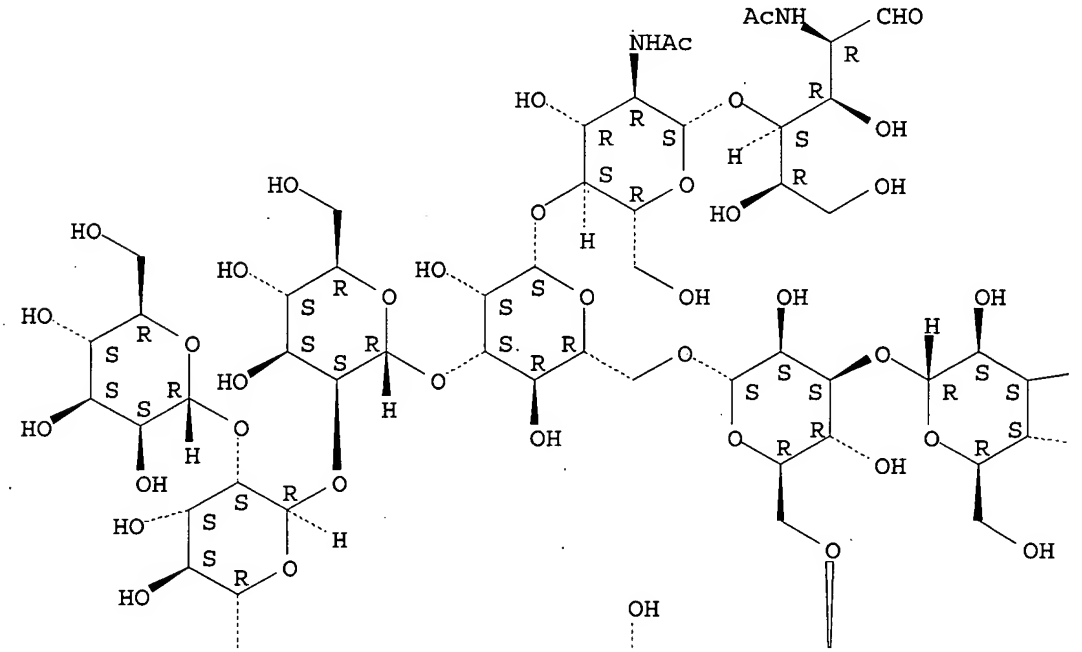


RN 208342-24-9 CAPLUS
CN D-Glucose, O-α-D-mannopyranosyl-(1→3)-O-[O-α-D-mannopyranosyl-(1→2)-6-O-phosphono-α-D-mannopyranosyl-(1→6)]-O-α-D-mannopyranosyl-(1→6)-O-[O-α-D-mannopyranosyl-(1→2)-O-6-O-phosphono-α-D-mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→3)]-O-β-D-mannopyranosyl-(1→4)-O-2-(acetylamino)-2-deoxy-β-D-glucopyranosyl-(1→4)-2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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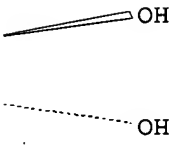

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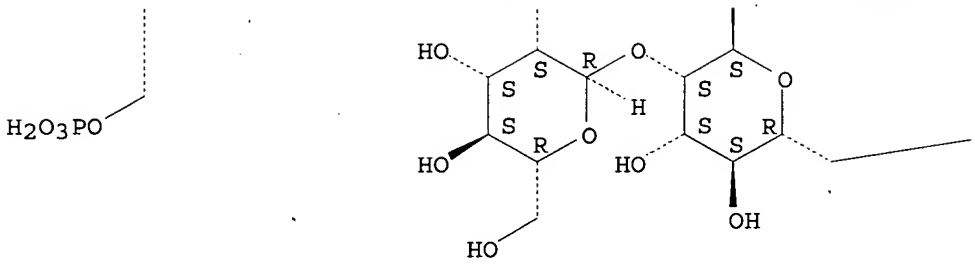


PAGE 2-B

—OPO_3H_2

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 13 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:58122 CAPLUS
DOCUMENT NUMBER: 124:108913
TITLE: Novel nucleic acid/substituted polyamine complexes, method for preparing same and use thereof for cell transfection
INVENTOR(S): Midoux, Patrick; Erbacher, Patrick; Roche-Degremont, Annie-Claude; Monsigny, Michel
PATENT ASSIGNEE(S): I.D.M. Immuno-Designed Molecules, Fr.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

Searched by Barb O'Bryen, STIC 2-2518

LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9530020	A1	19951109	WO 1995-FR535		19950424
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT					
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
FR 2719316	A1	19951103	FR 1994-5174		19940428
FR 2719316	B1	19960531			
US 5595897	A	19970121	US 1994-288681		19940810
CA 2187629	AA	19951109	CA 1995-2187629		19950424
CA 2187629	C	20040921			
AU 9524128	A1	19951129	AU 1995-24128		19950424
AU 695056	B2	19980806			
EP 753070	A1	19970115	EP 1995-918049		19950424
EP 753070	B1	20020925			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
AT 224957	E	20021015	AT 1995-918049		19950424
ES 2181775	T3	20030301	ES 1995-918049		19950424
PRIORITY APPLN. INFO.:			FR 1994-5174	A	19940428
			US 1994-288681	A2	19940810
			WO 1995-FR535	W	19950424

ED Entered STN: 30 Jan 1996

AB A polymer consisting of monomers containing free NH3+ groups, the free NH3+ functions being substituted in a ratio of at least 10%, advantageously 45-70% and particularly 60%, by uncharged residues causing a reduction in pos. charges relative to the unsubstituted polymer, is described. A complex consisting of at least one neg. charged nucleic acid and the described pos. charged polymer, and use of the complex for transfection of cells, are claimed. The substitution of the NH3+ groups reduces the pos. charge of the polymer and facilitates dissociation of nucleic acid within cells. The group conjugated to the amino group is not a recognition signal for a cell membrane receptor, but a fraction of the remaining amino groups may be conjugated to such a moiety to facilitate uptake of the nucleic acid/polymer complex by cells. Thus, polylysine was reacted with D-gluconolactone to produce polylysine in which .apprx.60% of the amino groups were masked with the sugar. This conjugates was further derivatized with lactose or with biotin. The polylysine-gluconic acid-lactose conjugate was complexed with a plasmid containing a luciferase gene. HepG2 cells were efficiently transfected using this complex. The effects of polylysine substitution on transfection efficiency were examined

IT **172787-61-0D, conjugates** with substituted polyamines
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(novel nucleic acid/substituted polyamine complexes and their use for cell transfection)

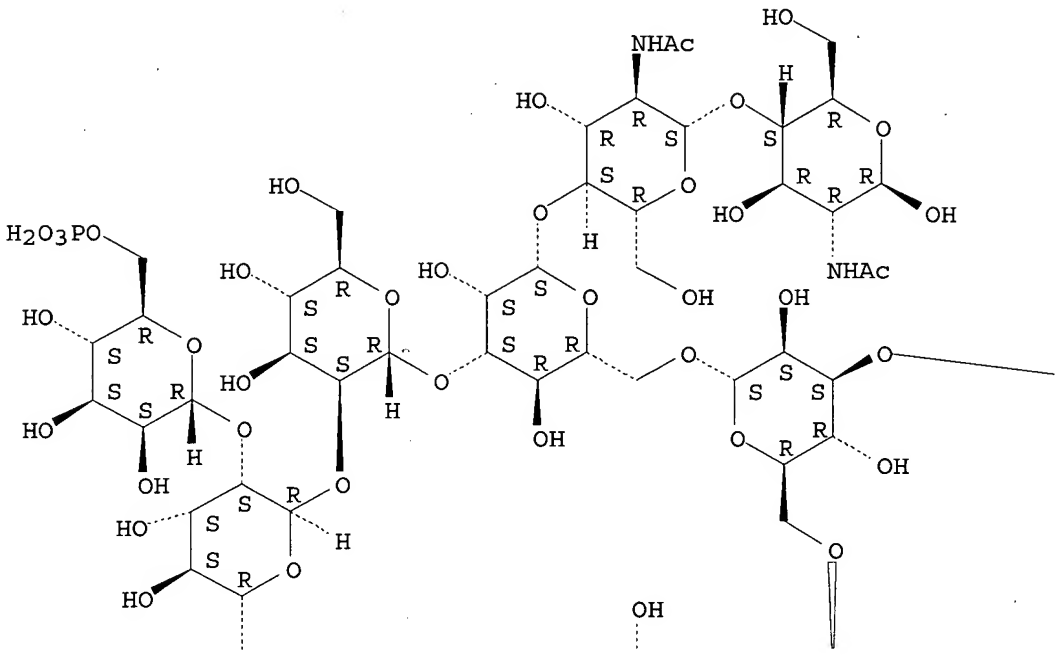
RN 172787-61-0 CAPLUS

CN β-D-Glucopyranose, O-α-D-mannopyranosyl-(1→3)-O-[O-6-O-phosphono-α-D-mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→6)]-O-α-D-mannopyranosyl-(1→6)-O-[O-6-O-phosphono-α-D-mannopyranosyl-(1→2)-O-α-D-mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→3)]-O-β-D-mannopyranosyl-(1→4)-O-2-(acetylamino)-2-deoxy-β-D-

glucopyranosyl-(1→4)-2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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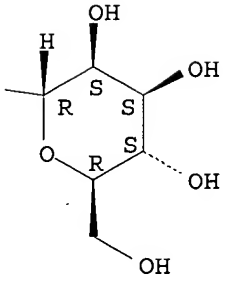
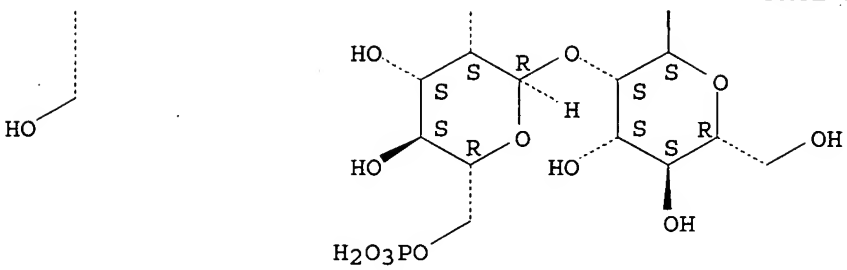


PAGE 2-A

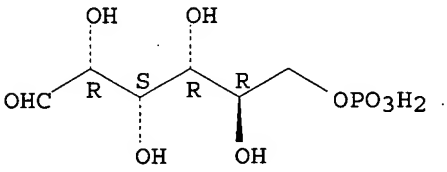


L74 ANSWER 14 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:655453 CAPLUS
DOCUMENT NUMBER: 123:80356
TITLE: Regulation of lysosomal and ubiquitin degradative pathways in differentiating human intestinal Caco-2 cells
AUTHOR(S): Zhang, Yan; Wick, Debra A.; Haas, Arthur L.; Seetharam, Bellur; Dahms, Nancy M.
CORPORATE SOURCE: Department of Biochemistry, Medical College of Wisconsin, Milwaukee, Wisconsin 53226, USA
SOURCE: Biochimica et Biophysica Acta (1995), 1267(1), 15-24
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 05 Jul 1995
AB The expression of various components of the lysosomal and ubiquitin-dependent degradative pathways was characterized in an in vitro model of differentiating enterocytes, the human colon adenocarcinoma Caco-2 cell line. The activities of the cell-associated lysosomal enzymes α-D-mannosidase, β-hexosaminidase, β-glucuronidase, and β-galactosidase increased .apprx.2- to 4-fold as differentiation proceeded. In contrast, the protein levels of the two mannose 6-phosphate receptors (MPRs), the insulin-like growth factor II/cation-independent MPR (IGF-II/CI-MPR) and the cation-dependent MPR (CD-MPR), did not change significantly during Caco-2 differentiation. In addition, quant. Western blot analyses revealed that on a molar basis the CD-MPR is 3.5 times more abundant than the IGF-II/CI-MPR in Caco-2 cells. Since only limited secretion of lysosomal enzymes was observed throughout differentiation, the level of expression of the MPRs was sufficient to target the increased levels of lysosomal enzymes to the lysosome. Unlike the expression of lysosomal enzymes, Western blot anal. demonstrated an .apprx.40% and .apprx.30% decrease, resp., in the steady-state levels of free and conjugated ubiquitin during Caco-2 differentiation. Taken together, these results show that the ubiquitin-dependent proteolytic pathway is regulated differently than the lysosomal degradative pathway during Caco-2 differentiation.

L74 ANSWER 15 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1987:513079 CAPLUS
DOCUMENT NUMBER: 107:113079
TITLE: Characteristics of **lysosomal** phosphomannosyl-enzyme receptors in the rat heart
AUTHOR(S): Marjomaki, V. S.; Salminen, A.
CORPORATE SOURCE: Dep. Cell Biol., Univ. Jyvaskyla, Jyvaskyla, SF-40100, Finland

SOURCE: Basic Research in Cardiology (1987), 82(3), 252-60
CODEN: BRCAB7; ISSN: 0300-8428
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 05 Oct 1987
AB The purpose of this study was to demonstrate the presence of a phosphomannosyl receptor system in rat heart muscle. The characterization of receptors was accomplished with β-N-acetylglucosaminidase (β-GA) secreted by rat embryo fibroblasts after NH4Cl stimulation. The receptor binding of ligand enzymes was saturated by adding increasing concns. of β-GA and the binding increased linearly when the content of membrane protein was increased. The binding of β-GA was inhibited by mannose and glucose phosphates, especially mannose 6-phosphate. Mannose itself did not inhibit binding of the enzyme, showing that the binding was not mediated by mannose receptors. Alkaline phosphatase treatment of β-GA decreased the binding of ligand enzymes to receptors. Alkaline conditions increased the dissociation of receptor-ligand complexes, whereas the dissociation was minimal between pH 5.5 and 6.5. The proportion of endogenous β-GA activity in membranes, probably representing a receptor-bound location, varied 40-55% of the total activity in various parts of rat cardiac muscle. The differences in the content of phosphomannosyl receptors, however, were insignificant between various cardiac muscle samples. At the organelle level the highest specific binding capacity, as well as the highest endogenous β-GA activity, was in the sarcolemmal fraction. Apparently, phosphomannosyl receptors also function in the endocytosis and transport of lysosomal enzymes in cardiomyocytes, as well as in several other cell types studied.
IT **56-73-5**
RL: BIOL (Biological study)
(**lysosomal** enzymes binding to phosphomannosyl receptors of heart sarcolemma inhibition by)
RN 56-73-5 CAPLUS
CN D-Glucose, 6-(dihydrogen phosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9012-33-3**, β-N-Acetylglucosaminidase
RL: PROC (Process)
(phosphomannosyl receptor binding of, in heart sarcolemma)
RN 9012-33-3 CAPLUS
CN Acetylhexosaminidase, β- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L74 ANSWER 16 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:467440 CAPLUS
DOCUMENT NUMBER: 103:67440
TITLE: **Lysosomal** enzyme binding to mouse P388D1 macrophage membranes lacking the 215-kDa mannose 6-phosphate receptor: Evidence for the existence of a second mannose 6-phosphate receptor
AUTHOR(S): Hoflack, Bernard; Kornfeld, Stuart

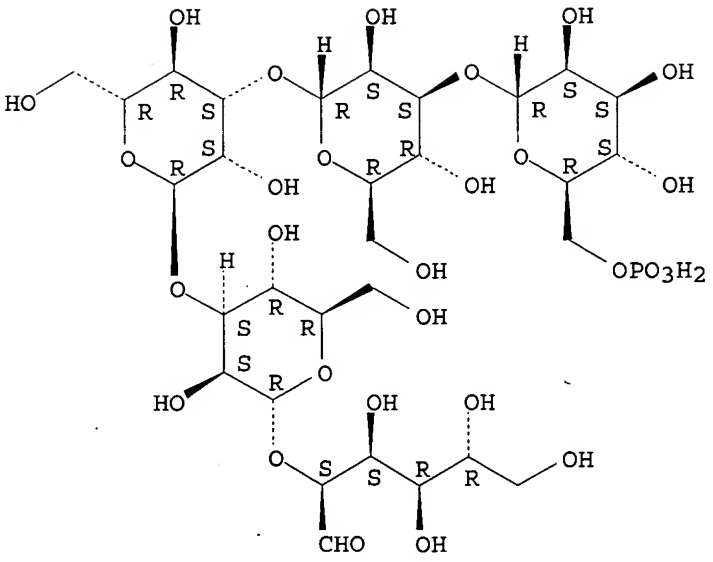
CORPORATE SOURCE: Sch. Med., Washington Univ., St. Louis, MO, 63110, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1985), 82(13), 4428-32
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 07 Sep 1985

AB Mouse P388D1 macrophages target newly synthesized acid hydrolases to lysosomes in spite of their lack of the 215-kilodalton (kDa) mannose 6-phosphate (Man-6-P) receptor. These cells contain a membrane-associated Man-6-P receptor that is distinct from the previously described receptor. The new receptor binds lysosomal enzymes containing phosphomannosyl residues. This binding is inhibited by Man-6-P or by pretreatment of the lysosomal enzymes with alkaline phosphatase. Lysosomal enzyme binding occurs at neutral pH and dissociation of the bound ligand occurs at low pH values comparable to those found within endosomes or lysosomes. The new receptor differs from the 215-kDa Man-6-P receptor in 2 ways. It has an absolute requirement for divalent cations and is unable to bind Dictyostelium discoideum lysosomal enzymes, which contain methylphosphomannosyl residues rather than the usual phosphomannosyl monoesters. Based on the difference in cation requirement, the 215-kDa receptor may be referred to as Man-6-P receptor CI (cation independent) and the new receptor as Man-6-P receptor CD (cation dependent). The Man-6-P receptor CD apparently functions in the targeting of newly synthesized acid hydrolases to lysosomes in P388D1 macrophages.

IT **9012-33-3**
RL: BIOL (Biological study)
(fibroblasts and macrophage membrane binding of, in human and lab animal, mannose phosphate receptors in relation to)
RN 9012-33-3 CAPLUS
CN Acetylhexosaminidase, β- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **72672-17-4**
RL: BIOL (Biological study)
(galactosidase binding by macrophage membranes inhibition by)
RN 72672-17-4 CAPLUS
CN D-Mannose, O-6-O-phosphono-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→2)- (9CI) (CA INDEX NAME)

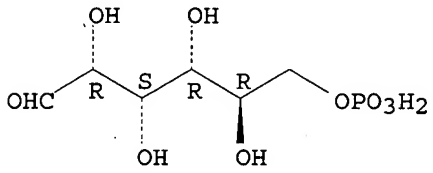
Absolute stereochemistry.



L74 ANSWER 17 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:60608 CAPLUS
DOCUMENT NUMBER: 102:60608
TITLE: Natural killer cell-mediated cytotoxicity does not depend on recognition of mannose 6-phosphate residues
AUTHOR(S): Haubeck, Hans Dieter; Kolesch, Eckehart; Imort, Michael; Hasilik, Andrej; Von Figura, Kurt
CORPORATE SOURCE: Hyg.-Inst., Univ. Muenster, Muenster, 4400, Fed. Rep. Ger.
SOURCE: Journal of Immunology (1985), 134(1), 65-9
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 24 Feb 1985
AB Interaction of mannose 6-phosphate-specific receptors with their ligands has been suggested to be essential for natural killer cell (NK)-mediated cytotoxicity. Indeed, mannose 6-phosphate-specific receptors and ligands bearing mannose 6-phosphate residues are demonstrable on human peripheral blood leukocytes with NK activity as well as on K-562 NK target cells, allowing at least in principle such an interaction. It can also be shown that NK activity of human peripheral blood leukocytes is inhibited by mannose 6-phosphate. The following observations, however, exclude an essential role of the mannose 6-phosphate receptor-ligand system in NK cell-mediated cytotoxicity. 1) NK cytotoxicity is sensitive to a broad range of structurally unrelated sugar phosphates. 2) NK activity is normal in patients with 1 cell disease (mucolipidosis II), which, due to a genetic defect are unable to synthesize the ligands for the mannose-6-phosphate-specific receptor. 3) NK cytotoxicity is not inhibited by an antiserum against the mannose 6-phosphate receptor, which blocks the receptor function.
IT **9012-33-3**
RL: BIOL (Biological study)
(natural killer lymphocyte cytotoxicity in relation to, of humans)
RN 9012-33-3 CAPLUS
CN Acetylhexosaminidase, β- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **56-73-5**
RL: BIOL (Biological study)
(natural killer lymphocyte cytotoxicity inhibition by, of humans)
RN 56-73-5 CAPLUS
CN D-Glucose, 6-(dihydrogen phosphate) (8CI, 9CI) (CA INDEX NAME)

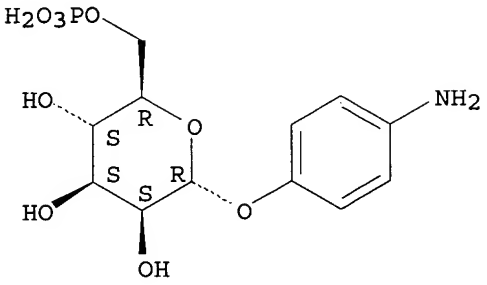
Absolute stereochemistry.



L74 ANSWER 18 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:528325 CAPLUS
DOCUMENT NUMBER: 93:128325
TITLE: p-Isothiocyanatophenyl 6-phospho-α-D-mannopyranoside **coupled** to albumin. A model compound recognized by the fibroblast **lysosomal** enzyme uptake system. 1. Chemical synthesis and characterization
AUTHOR(S): Sando, Gloria N.; Karson, Evelyn M.
CORPORATE SOURCE: Dep. Intern. Med., Univ. Iowa, Iowa City, IA, 52242, USA
SOURCE: Biochemistry (1980), 19(16), 3850-5
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
AB A simple synthesis for a conjugate of albumin and p-aminophenyl 6-phospho-α-D-mannopyranoside (I) was developed to study the requirements of the fibroblast lysosomal enzyme recognition system. I was prepared in 2 ways: (1) phosphorylation of p-nitrophenyl α-D-mannopyranoside and subsequent reduction of the NO2 group by catalytic hydrogenation, and (2) direct phosphorylation of p-aminophenyl α-D-mannopyranoside. Mannosides were phosphorylated in a reaction with phosphoryl chloride, pyridine, and H2O at 0° for 1 h, by a procedure selective for primary OH groups. Purified I was characterized by chromatog., enzymic, and 13C NMR spectroscopic methods. p-Isothiocyanatophenyl 6-phospho-α-D-mannopyranoside as well as the p-isothiocyanatophenyl glycosides of α-mannose, α-glucose, α- and β-galactose, and α-L-fucose were formed by reaction of the resp. p-aminophenyl glycosides with thiophosgene. Incubation of the p-isothiocyanatophenyl glycosides with bovine serum albumin at pH 8.5, 25°, for 18 h generally resulted in the coupling, primarily through lysine residues, of ≤20-30 mol of glycoside/mol of protein. Biol. properties of the conjugates in the fibroblast lysosomal enzyme recognition system are described in the accompanying paper (Karson, E. M., et al., 1980).
IT **74160-60-4P**
RL: PREP (Preparation)
(preparation and **coupling** to albumin)
RN 74160-60-4 CAPLUS
CN α-D-Mannopyranoside, 4-aminophenyl, 6-(dihydrogen phosphate) (9CI) (CA INDEX NAME)

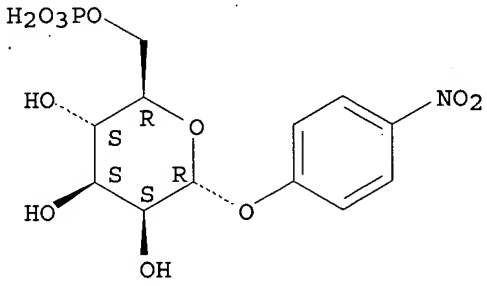
different method of coupling

Absolute stereochemistry.



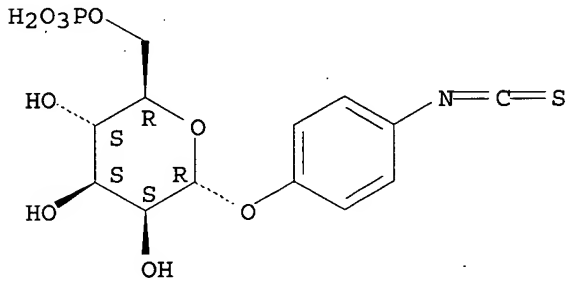
IT **74141-14-3P**
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)
RN 74141-14-3 CAPLUS
CN α-D-Mannopyranoside, 4-nitrophenyl, 6-(dihydrogen phosphate) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



IT **74141-15-4DP**, albumin complexes
RL: PREP (Preparation)
(preparation of, from aminophenyl phosphomannoside, **lysosomal**
enzyme uptake system in relation to)
RN 74141-15-4 CAPLUS
CN α-D-Mannopyranoside, 4-isothiocyanatophenyl, 6-(dihydrogen
phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

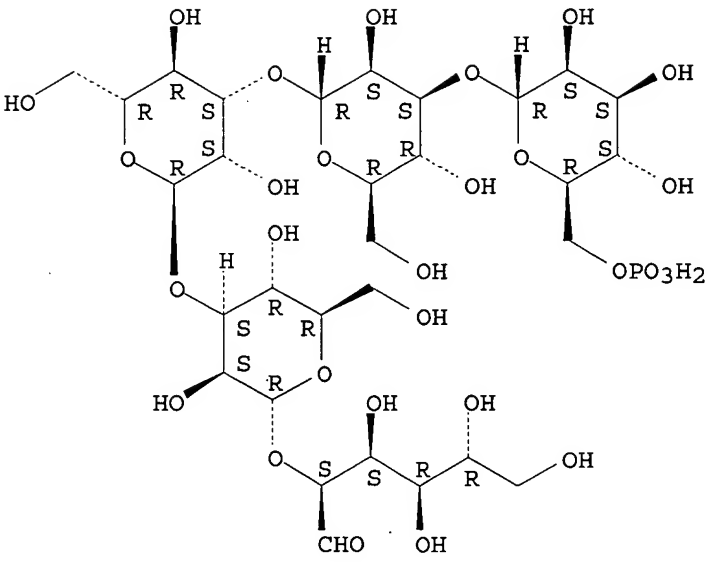


L74 ANSWER 19 OF 41 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1980:105076 CAPLUS
DOCUMENT NUMBER: 92:105076
TITLE: Fibroblast receptor for **lysosomal** enzymes mediates pinocytosis of multivalent phosphomannan fragment
AUTHOR(S): Fischer, H. David; Natowicz, Marvin; Sly, William S.; Bretthauer, Roger K.
CORPORATE SOURCE: Sch. Med., Washington Univ., St. Louis, MO, USA
SOURCE: Journal of Cell Biology (1980), 84(1), 77-86
CODEN: JCLBA3; ISSN: 0021-9525
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
AB Mild acid hydrolysis of phosphomannan [9044-08-0] secreted by the yeast Hansenula holstii (NRRLY-2448) produced 2 phosphomannosyl fragments which differed strikingly in their potency as inhibitors of pinocytosis of human β-glucuronidase [**9001-45-0**] by human fibroblasts. The larger mol. weight polyphosphomonoester fragment was 100,000-fold more potent an inhibitor of enzyme uptake than the smaller pentamannosyl monophosphate [**72672-17-4**] fragment. Binding to attached fibroblasts at 3° was much greater with the polyphosphomonoester fragment than with the pentamannosyl monophosphate. The larger mol. weight fragment was also subject to adsorptive pinocytosis and was taken up by fibroblasts at a rate 30-fold greater than the rate of uptake of pentamannosyl monophosphate. Evidence that the polyphosphomonoester fragment was taken up by the phosphomannosyl-recognition system that mediates uptake of lysosomal enzymes included: (a) its pinocytosis was inhibited by the same compds. that competitively inhibit enzyme pinocytosis (mannose 6-phosphate and phosphomannan from Saccharomyces cerevisiae mutant mnn-1); (b) alkaline phosphatase treatment greatly reduced its susceptibility to pinocytosis; (c) its pinocytosis was competitively inhibited by high-uptake human β-glucuronidase; and (d) this inhibition by high-uptake enzyme was dramatically reduced by prior treatment of the enzyme with alkaline phosphatase or endoglycosidase-H. Endoglycosidase-H treatment of human β-glucuronidase dramatically reduced its susceptibility to pinocytosis by fibroblasts. The phosphomannosyl components of high-uptake enzyme released by endoglycosidase-H treatment were much less effective inhibitors of polyphosphomonoester pinocytosis than when present on the phosphomannosyl-enzyme. High-uptake acid hydrolases may be polyvalent ligands analogous to the polyphosphomonoester mannan fragment whose pinocytosis depends on interaction of >1 phosphomannosyl recognition marker with pinocytosis receptors on fibroblasts.
IT **9001-45-0**
RL: PRP (Properties)
(pinocytosis of, by fibroblast, phosphomannan fragments effect on)
RN 9001-45-0 CAPLUS
CN Glucuronidase, β- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **72672-17-4**
RL: PRP (Properties)
(pinocytosis response to, in fibroblast)
RN 72672-17-4 CAPLUS
CN D-Mannose, O-6-O-phosphono-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→3)-O-α-D-mannopyranosyl-(1→2)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L74 ANSWER 20 OF 41 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2004605202 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15383547
TITLE: **Conjugation** of **mannose** 6-**phosphate**-containing oligosaccharides to acid alpha-glucosidase improves the clearance of glycogen in pompe mice.
AUTHOR: Zhu Yunxiang; Li Xuemei; Kyazike Josephine; Zhou Qun; Thurberg Beth L; Raben Nina; Mattaliano Robert J; Cheng Seng H
CORPORATE SOURCE: Genzyme Corporation, Framingham, Massachusetts 01701-9322, USA.
SOURCE: Journal of biological chemistry, (2004 Nov 26) 279 (48) 50336-41. Electronic Publication: 2004-09-21.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 20041207
Last Updated on STN: 20050208
Entered Medline: 20050207

ABSTRACT:
Clinical studies of enzyme replacement therapy for Pompe disease have indicated that relatively high doses of recombinant human acid alpha-glucosidase (rhGAA)

may be required to reduce the abnormal glycogen storage in cardiac and skeletal muscles. This may be because of inefficient cation-independent mannose 6-phosphate receptor (CI-MPR)-mediated endocytosis of the enzyme by the affected target cells. To address this possibility, we examined whether the addition of a high affinity ligand to rhGAA would improve its delivery to these cells. Chemical conjugation of high mannose oligosaccharides harboring mono- and bisphosphorylated mannose 6-phosphates onto rhGAA (neo-rhGAA) significantly improved its uptake characteristics by muscle cells in vitro. Infusion of neo-rhGAA into Pompe mice also resulted in greater delivery of the enzyme to muscle tissues when compared with the unmodified enzyme. Importantly, this increase in enzyme levels was associated with significantly improved clearance of glycogen (approximately 5-fold) from the affected tissues. These results suggest that CI-MPR-mediated endocytosis of rhGAA is an important pathway by which the enzyme is delivered to the affected **lysosomes** of Pompe muscle cells. Hence, the generation of rhGAA containing high affinity ligands for the CI-MPR represents a strategy by which the potency of rhGAA and therefore the clinical efficacy of enzyme replacement therapy for Pompe disease may be improved.

CONTROLLED TERM: Animals
Disease Models, Animal
*Glycogen: ME, metabolism
*Glycogen Storage Disease Type II: ME, metabolism
*Mannosephosphates: ME, metabolism
Mice
Muscles: ME, metabolism
Myoblasts: ME, metabolism
*Oligosaccharides: ME, metabolism
Protein Transport: PH, physiology
*alpha-Glucosidases: ME, metabolism
CAS REGISTRY NO.: 3672-15-9 (mannose-6-phosphate); 9005-79-2 (Glycogen)
CHEMICAL NAME: 0 (Mannosephosphates); 0 (Oligosaccharides); EC 3.2.1.20 (alpha-Glucosidases)

L74 ANSWER 21 OF 41 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2004137572 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15031649
TITLE: Partial purification and characterization of a mannosyl transferase involved in O -linked mannosylation of glycoproteins in Candida albicans.
AUTHOR: Arroyo-Flores Blanca L; Calvo-Mendez Carlos; Flores-Carreon Arturo; Lopez-Romero Everardo
CORPORATE SOURCE: Instituto de Investigacion en Biologia Experimental, Facultad de Quimica, Universidad de Guanajuato, Apdo. Postal No. 187, Guanajuato, Gto. 36000, Mexico.
SOURCE: Antonie van Leeuwenhoek, (2004 Apr) 85 (3) 199-207. Journal code: 0372625. ISSN: 0003-6072.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20040320
Last Updated on STN: 20040618
Entered Medline: 20040617

ABSTRACT:
Incubation of a mixed membrane fraction of C. albicans with the nonionic detergents Nonidet P-40 or Lubrol solubilized a fraction that catalyzed the transfer of mannose either from endogenously generated or exogenously added dolichol-P-[14C]Man onto endogenous protein acceptors. The protein mannosyl transferase solubilized with Nonidet P-40 was partially purified by a single

step of preparative nondenaturing electrophoresis and some of its properties were investigated. Although transfer activity occurred in the absence of exogenous mannose acceptors and thus depended on acceptor proteins isolated along with the enzyme, addition of the protein fraction obtained after chemical de-mannosylation of glycoproteins synthesized in vitro stimulated mannoprotein labeling in a concentration-dependent manner. Other de-mannosylated glycoproteins, such as yeast invertase or glycoproteins extracted from C. albicans, failed to increase the amount of labeled mannoproteins. Mannosyl transfer activity was not influenced by common metal ions such as Mg(2+), Mn(2+) and Ca(2+), but it was stimulated up to 3-fold by EDTA. Common phosphoglycerides such as phosphatidylglycerol and, to a lower extent, phosphatidylinositol and phosphatidylcholine enhanced transfer activity. Interestingly, **coupled** transfer activity between dolichol ***phosphate*** **mannose** synthase, i.e., the **enzyme** responsible for Dol-P-Man synthesis, and protein mannosyl transferase could be reconstituted in vitro from the partially purified transferases, indicating that this process can occur in the absence of cell membranes.

CONTROLLED TERM: *Candida albicans: ME, metabolism
Cell Membrane: ME, metabolism
Detergents: CH, chemistry
Dolichol Phosphates: ME, metabolism
Fungal Proteins: IP, isolation & purification
*Fungal Proteins: ME, metabolism
*Glycoproteins: ME, metabolism
Glycosylation
Mannose: CH, chemistry
Mannose: ME, metabolism
*Mannosyltransferases: IP, isolation & purification
*Mannosyltransferases: ME, metabolism
Membrane Proteins: IP, isolation & purification
Membrane Proteins: ME, metabolism
Phospholipids: ME, metabolism
Research Support, Non-U.S. Gov't

CAS REGISTRY NO.: 31103-86-3 (Mannose)

CHEMICAL NAME: 0 (Detergents); 0 (Dolichol Phosphates); 0 (Fungal Proteins); 0 (Glycoproteins); 0 (Membrane Proteins); 0 (Phospholipids); EC 2.4.1. (Mannosyltransferases)

L74 ANSWER 22 OF 41 MEDLINE on STN DUPLICATE 7

ACCESSION NUMBER: 2001111656 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11152512

TITLE: Adenovirus serotype 7 retention in a late endosomal compartment prior to cytosol escape is modulated by fiber protein.

AUTHOR: Miyazawa N; Crystal R G; Leopold P L

CORPORATE SOURCE: Division of Pulmonary and Critical Care Medicine, Weill Medical College of Cornell University, New York, New York 10021, USA.

CONTRACT NUMBER: P01 HL51746-06A1 (NHLBI)
P01 HL59312 (NHLBI)
R29AI 42250 (NIAID)

SOURCE: Journal of virology, (2001 Feb) 75 (3) 1387-400.
Journal code: 0113724. ISSN: 0022-538X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200102

ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322

Entered Medline: 20010202

ABSTRACT:
The intracellular trafficking of adenovirus (Ad) subgroup B (e.g., Ad7) differs from that of subgroup C (e.g., Ad5) in that Ad5 rapidly escapes from endocytic compartments following infection whereas Ad7 accumulates in organelles. To assess the hypothesis that Ad7 is targeted to the **lysosomal** pathway, Ad7 and Ad5 were **conjugated** with fluorophores and their trafficking in A549 epithelial cells was analyzed by fluorescence microscopy. Within 1 h after infection, Ad7, but not Ad5, accumulated in the cytoplasm of A549 cells. The pH in the environment of Ad5 was nearly neutral (pH 7), while Ad7 occupied acidic compartments (pH 5) over the first 2 h with a gradual shift toward neutrality by 8 h. Ad7 partially colocalized with alpha(2)-macroglobulin and late endosomal and lysosomal marker proteins, including Rab7, **mannose** -6- **phosphate** receptor, and LAMP-1. The pH optimum for membrane lysis by Ad7, as well as a chimeric Ad5 capsid that expressed the Ad7 fiber (Ad5fiber7), was pH 5.5, while that for lysis by Ad5 was pH 6.0. Thus, the native trafficking pathway for Ad7 involves residence in late endosomes and lysosomes, with information encoded in the Ad7 fiber acting as a pH-dependent trigger for membrane lysis and escape to the cytosol.

CONTROLLED TERM: *Adenoviridae: PH, physiology
Antigens, CD: AN, analysis
*Capsid: PH, physiology
*Capsid Proteins
Cell Line
Cell Nucleus: VI, virology
DNA, Viral: ME, metabolism
*Endosomes: VI, virology
Gene Therapy
Humans
Hydrogen-Ion Concentration
Lysosomes: VI, virology
Membrane Glycoproteins: AN, analysis
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Serotyping
alpha-Macroglobulins: PD, pharmacology

CHEMICAL NAME: 0 (Antigens, CD); 0 (Capsid Proteins); 0 (DNA, Viral); 0 (Membrane Glycoproteins); 0 (alpha-Macroglobulins); 0 (hexon capsid protein, Adenovirus); 0 (lysosome-associated membrane glycoproteins)

L74 ANSWER 23 OF 41 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 1998017825 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9378754
TITLE: Dense core **lysosomes** can fuse with late endosomes and are re-formed from the resultant hybrid organelles.
AUTHOR: Bright N A; Reaves B J; Mullock B M; Luzio J P
CORPORATE SOURCE: Department of Clinical Biochemistry, University of Cambridge, Addenbrooke's Hospital, UK.
SOURCE: Journal of cell science, (1997 Sep) 110 (Pt 17) 2027-40.
Journal code: 0052457. ISSN: 0021-9533.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 20020420
Entered Medline: 19971107

ABSTRACT:

Electron microscopy was used to evaluate the function and formation of dense core **lysosomes. Lysosomes** were preloaded with bovine serum albumin (BSA)-gold conjugates by fluid phase endocytosis using a pulse-chase protocol. The gold particles present in dense core **lysosomes** and late endosomes were flocculated, consistent with proteolytic degradation of the BSA. A second pulse of BSA-gold also accumulated in the pre-loaded dense core ***lysosomes*** at 37 degrees C, but accumulation was reversibly blocked by incubation at 20 degrees C. Time course experiments indicated that mixing of the two BSA-gold **conjugates** initially occurred upon fusion of ***mannose*** 6-**phosphate** receptor-positive/**lysosomal** glycoprotein-positive late endosomes with dense core **lysosomes.** Treatment for 5 hours with wortmannin, a phosphatidyl inositide 3-kinase inhibitor, caused a reduction in number of dense core **lysosomes** preloaded with BSA-gold and prevented a second pulse of BSA-gold accumulating in them. After wortmannin treatment the two BSA-gold conjugates were mixed in swollen late endosomal structures. Incubation of NRK cells with 0.03 M sucrose resulted in the formation of swollen sucrosomes which were morphologically distinct from preloaded dense core **lysosomes** and were identified as late endosomes and hybrid endosome-**lysosome** structures. Subsequent endocytosis of invertase resulted in digestion of the sucrose and re-formation of dense core **lysosomes.** These observations suggest that dense core ***lysosomes*** are biologically active storage granules of **lysosomal** proteases which can fuse with late endosomes and be re-formed from the resultant hybrid organelles prior to subsequent cycles of fusion and re-formation.

CONTROLLED TERM:
Androstadienes: PD, pharmacology
Animals
Antigens, CD: AN, analysis
Cathepsins: AN, analysis
Cells, Cultured
Endocytosis: DE, drug effects
*Endocytosis: PH, physiology
*Endopeptidases
Endosomes: CH, chemistry
*Endosomes: PH, physiology
Endosomes: UL, ultrastructure
Enzyme Inhibitors: PD, pharmacology
Enzyme Precursors: AN, analysis
Fibroblasts: CY, cytology
Fibroblasts: EN, enzymology
Fibroblasts: UL, ultrastructure
Glycoside Hydrolases: PK, pharmacokinetics
Gold: PK, pharmacokinetics
Hydrolases: ME, metabolism
Kidney: CY, cytology
Lysosomes: CH, chemistry
***Lysosomes: PH, physiology**
Lysosomes: UL, ultrastructure
Membrane Glycoproteins: AN, analysis
Microscopy, Immunoelectron
Rats
Receptor, IGF Type 2: AN, analysis
Research Support, Non-U.S. Gov't
Serum Albumin, Bovine: PK, pharmacokinetics
Sucrose: PK, pharmacokinetics
beta-Fructofuranosidase

CAS REGISTRY NO.: 19545-26-7 (wortmannin); 57-50-1 (Sucrose); 7440-57-5 (Gold)

CHEMICAL NAME: 0 (Androstadienes); 0 (Antigens, CD); 0 (Enzyme Inhibitors); 0 (Enzyme Precursors); 0 (Membrane

Glycoproteins); 0 (Receptor, IGF Type 2); 0 (Serum Albumin, Bovine); 0 (**lysosome**-associated membrane glycoproteins); EC 3. (Hydrolases); EC 3.2.1. (Glycoside Hydrolases); EC 3.2.1.26 (beta-Fructofuranosidase); EC 3.4.- (Cathepsins); EC 3.4.- (Endopeptidases); EC 3.4.22.- (cathepsin L, rat); EC 3.4.22.- (cathepsin L, transformed mouse fibroblasts); EC 3.4.22.15 (cathepsin L)

L74 ANSWER 24 OF 41 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 96030727 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7562256
TITLE: The abnormal isoform of the prion protein accumulates in late-endosome-like organelles in scrapie-infected mouse brain.
AUTHOR: Arnold J E; Tipler C; Laszlo L; Hope J; Landon M; Mayer R J
CORPORATE SOURCE: Department of Biochemistry, University of Nottingham Medical School, Queen's Medical Centre, U.K.
SOURCE: Journal of pathology, (1995 Aug) 176 (4) 403-11. Journal code: 0204634. ISSN: 0022-3417.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19951227
Last Updated on STN: 19951227
Entered Medline: 19951114

ABSTRACT:
The prion encephalopathies are characterized by accumulation in the brain of the abnormal form PrPsc of a normal host gene product PrPc. The mechanism and site of formation of PrPsc from PrPc are currently unknown. In this study, ME7 scrapie-infected mouse brain was used to show, both biochemically and by double-labelled immunogold electron microscopy, that proteinase K-resistant PrPsc is enriched in subcellular structures which contain the cation-independent **mannose** 6-**phosphate** receptor, ubiquitin-protein **conjugates**, beta-**glucuronidase**, and cathepsin B, termed late endosome-like organelles. The glycosylinositol phospholipid membrane-anchored PrPc will enter such compartment for normal degradation and the organelles may therefore act as chambers for the conversion of PrPc into infectious PrPsc in this murine model of scrapie.

CONTROLLED TERM: Animals
Blotting, Western
*Brain: ME, metabolism
Brain: UL, ultrastructure
*Endosomes: ME, metabolism
Mice
Mice, Inbred C57BL
Microscopy, Electron
Prions: CH, chemistry
*Prions: ME, metabolism
Research Support, Non-U.S. Gov't
*Scrapie: ME, metabolism
Scrapie: PA, pathology
CHEMICAL NAME: 0 (Prions)

L74 ANSWER 25 OF 41 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 94243123 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8186546
TITLE: Interactions of HIV-1 and HIV-2 envelope glycoproteins with sulphated polysaccharides and **mannose**-6-

phosphate.

AUTHOR: Mbemba E; Gluckman J C; Gattegno L
CORPORATE SOURCE: Laboratoire de Biologie Cellulaire, Faculte de Medecine Paris-Nord, Bobigny, France.
SOURCE: Glycobiology, (1994 Feb) 4 (1) 13-21.
Journal code: 9104124. ISSN: 0959-6658.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940629
Last Updated on STN: 19970203
Entered Medline: 19940623

ABSTRACT:
Envelope glycoproteins of human immunodeficiency viruses (HIV-1 and HIV-2) can interact with high-mannose glycans and with the mannosyl or N-acetylglucosaminyl core of complex-type oligosaccharidic structures. HIV-1 glycoproteins also specifically bind sulphated polysaccharides such as dextran sulphate (DS) and heparin. Here, we show that the latter property is shared by HIV-2 recombinant gp140 (rgp140) precursor glycoprotein. Binding of rgp140 and of corresponding rgp160 of HIV-1 to heparin- and DS-substituted (sulphated dextran beads; SDB) affinity matrices was inhibited by the soluble specific ligand and also by fetuin, asialofetuin or the anionic simple carbohydrate derivative **mannose-6-phosphate (M6P)**.
Interaction of HIV-1 rgp120 subunit with the two affinity matrices was also inhibited by **M6P**, but only rgp120 binding to heparin-agarose, and not that to SDB, was affected by fetuin and asialofetuin. These results suggest that HIV-1 and HIV-2 envelope glycoproteins presumably display different sulphated polysaccharide and carbohydrate recognition sites. Some of these may be common or in close proximity: with respect to rgp160, for example, the sites may be common on the gp41 moiety and/or in a region of gp120 which would be more accessible when expressed on rgp160 than on processed gp120, while they may be distinct on the cleaved gp120 subunit. Finally, because **M6P** is a marker of lysosomal **enzymes**, we verified that HIV-1 and HIV-2 envelope glycoproteins could specifically bind in a **M6P**-inhibitable manner to a representative **lysosomal enzyme**, bovine liver beta-**glucuronidase coupled** to agarose, suggesting that they may possibly interfere with lysosomal enzyme sorting in HIV-infected cells.

CONTROLLED TERM:
Animals
Binding Sites
Cattle
Dextran Sulfate: CH, chemistry
*Dextran Sulfate: ME, metabolism
*Gene Products, env: ME, metabolism
Glucuronidase: ME, metabolism
*HIV-1: ME, metabolism
*HIV-2: ME, metabolism
*Heparin: ME, metabolism
Liver: EN, enzymology
*Mannosephosphates: ME, metabolism
Protein Binding
Research Support, Non-U.S. Gov't
Sepharose: AA, analogs & derivatives
Sepharose: ME, metabolism
CAS REGISTRY NO.: **3672-15-9 (mannose-6-phosphate)**; 9005-49-6 (Heparin); 9012-36-6 (Sepharose); 9042-14-2 (Dextran Sulfate)
CHEMICAL NAME: 0 (Gene Products, env); 0 (Mannosephosphates); 0 (heparin-sepharose); EC 3.2.1.31 (Glucuronidase)

L74 ANSWER 26 OF 41 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 90062165 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2584220
TITLE: Phosphorylation of lignin peroxidases from Phanerochaete chrysosporium. Identification of mannose 6-phosphate.
AUTHOR: Kuan I C; Tien M
CORPORATE SOURCE: Department of Molecular and Cell Biology, Pennsylvania State University, University Park 16802.
CONTRACT NUMBER: 1-P42ES04922-01 (NIEHS)
SOURCE: Journal of biological chemistry, (1989 Dec 5) 264 (34) 20350-5.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199001
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 19970203
Entered Medline: 19900108
ABSTRACT:
Many of the extracellular lignin-degrading peroxidases from the wood-degrading fungus Phanerochaete chrysosporium are phosphorylated. Immunoprecipitation of the extracellular fluid of cultures grown with H2K32PO4 with a polyclonal antibody raised against one of the lignin peroxidase isozymes, H8 (pI 3.5), revealed the incorporation of H2K32PO4 into lignin peroxidases. Analyses of the purified isozymes from labeled cultures by isoelectric focusing showed that, in addition to isozyme H8, lignin peroxidase isozymes H2 (pI 4.4), H6 (pI 3.7), and H10 (pI 3.3) are also phosphorylated. These analyses also showed that lignin peroxidase isozyme H1 (pI 4.7) and manganese-dependent peroxidase isozymes H3 (pI 4.9) and H4 (pI 4.5) are not phosphorylated. Phosphate quantitation indicated the presence of one molecule of phosphate/molecule of enzyme for all of the phosphorylated isozymes. To locate the site of phosphorylation, one-dimensional phosphoamino acid analysis was performed with hydrolyzed 32P-protein. However, phosphotyrosine, phosphoserine, and phosphothreonine could not be identified. **Coupled enzyme** assays of acid hydrolysate indicated the presence of **mannose** 6-***phosphate*** as the phosphorylated component on the lignin peroxidase isozymes. Digestion of the isozymes with N-glycanase released the phosphate component, indicating that the mannose 6-phosphate is contained on an asparagine-linked oligosaccharide.
CONTROLLED TERM: *Agaricales: EN, enzymology
Amino Acids: AN, analysis
*Hexosephosphates: ME, metabolism
Isoenzymes: IP, isolation & purification
*Isoenzymes: ME, metabolism
Mannosephosphates: IP, isolation & purification
*Mannosephosphates: ME, metabolism
Peroxidases: IP, isolation & purification
*Peroxidases: ME, metabolism
Phosphorylation
Research Support, U.S. Gov't, Non-P.H.S.
Research Support, U.S. Gov't, P.H.S.
CAS REGISTRY NO.: 3672-15-9 (mannose-6-phosphate)
CHEMICAL NAME: 0 (Amino Acids); 0 (Hexosephosphates); 0 (Isoenzymes); 0 (Mannosephosphates); EC 1.11.1. (Peroxidases); EC 1.11.1.- (lignin peroxidase)

L74 ANSWER 27 OF 41 MEDLINE on STN DUPLICATE 14

ACCESSION NUMBER: 89227193 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2540710
TITLE: **Lysosomal** integral membrane glycoproteins are expressed at high levels in the inclusion bodies of I-cell disease fibroblasts.
AUTHOR: Sandoval I V; Chen J W; Yuan L; August J T
CORPORATE SOURCE: Cell Biology and Metabolism Branch, National Institute of Child Health and Human Development, Bethesda, Maryland 20892.
CONTRACT NUMBER: 5 R01 GM31168 (NIGMS)
5 T32 GM07309 (NIGMS)
SOURCE: Archives of biochemistry and biophysics, (1989 May 15) 271 (1) 157-67.
Journal code: 0372430. ISSN: 0003-9861.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198906
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 20000303
Entered Medline: 19890607

ABSTRACT:
The localization, expression, and transport of two **lysosomal** integral membrane glycoproteins of human cells, hLAMP-1 and hLAMP-2, have been studied in mucolipidosis II (I-cell disease) fibroblasts. These cells are deficient in N-acetylglucosaminylphosphotransferase, one of the enzymes required for addition of the mannose 6-phosphate recognition signal to newly synthesized ***lysosomal*** hydrolases and a prerequisite for the sorting and transport of the hydrolases to **lysosomes.** I-cells analyzed by immunofluorescence microscopy with monoclonal antibodies against hLAMP-1 and hLAMP-2 showed intense staining of the inclusion bodies covering most of the cytoplasm of the cells. Immunoelectron microscopy confirmed this localization and showed that the hLAMP-positive vesicles commonly contained membrane structures or electron-dense homogeneous material characteristic of secondary ***lysosomes.*** Studies of the biosynthesis of hLAMP-2 in I-cells pulse-labeled with [35S]methionine indicated that the molecule is glycosylated in the Golgi system, is transported to vesicles with the high density characteristic of **lysosomes**, and has chemical properties similar to those of the glycoprotein synthesized in normal cells. The concentration of the hLAMP-2 glycoprotein was three- to fourfold greater than that in normal fibroblasts, in sharp contrast to the reduced levels of **lysosomal** hydrolases seen in I-cells. These experiments demonstrate that the inclusion bodies in I-cells have properties of secondary **lysosomes** and that the transport and targeting of the **lysosomal** membrane glycoproteins to the inclusion bodies of these cells is not **coupled** to the ***mannose*** 6-**phosphate** system for transporting soluble acid hydrolases.

CONTROLLED TERM: Check Tags: Comparative Study
*Antigens, CD
Biological Transport
Cell Line
Fibroblasts: ME, metabolism
Fluorescent Antibody Technique
Golgi Apparatus: ME, metabolism
Humans
Hydrolases: ME, metabolism
*Inclusion Bodies: ME, metabolism
Inclusion Bodies: UL, ultrastructure
***Lysosomes: ME, metabolism**

Lysosomes: UL, ultrastructure
*Membrane Glycoproteins: BI, biosynthesis
Membrane Glycoproteins: ME, metabolism
Microscopy, Fluorescence
*Mucolipidoses: ME, metabolism
Research Support, U.S. Gov't, Non-P.H.S.
Research Support, U.S. Gov't, P.H.S.
CHEMICAL NAME: 0 (Antigens, CD); 0 (Membrane Glycoproteins); 0 (**lysosome**-associated membrane glycoproteins); EC 3. (Hydrolases)

L74 ANSWER 28 OF 41 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 90126864 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2558886
TITLE: Transferrin receptors and cation-independent mannose-6-phosphate receptors deliver their ligands to two distinct subpopulations of multivesicular endosomes.
AUTHOR: Woods J W; Goodhouse J; Farquhar M G
CORPORATE SOURCE: Department of Cell Biology, Yale University School of Medicine, New Haven, CT 06510-8002.
CONTRACT NUMBER: CA46128 (NCI)
DK17780 (NIDDK)
SOURCE: European journal of cell biology, (1989 Oct) 50 (1) 132-43. Journal code: 7906240. ISSN: 0171-9335.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199002
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 20000303
Entered Medline: 19900228

ABSTRACT:
The distribution of transferrin receptors (Tf-R) was determined in Clone 9 hepatocytes and compared to that of 215 kDa, cation-independent mannose-6-phosphate receptors (M6P-R) by double labeling. Cells were allowed to take up exogenous human transferrin (Tf) for 5 to 30 min, after which Tf, Tf-R, and M6P-R were localized by immunofluorescence using specific antibodies. All these proteins were found to be concentrated in the juxtanuclear or Golgi region. When Clone 9 cells were treated with NH4Cl to trap M6P-R in endosomes (Brown, W. J., J. Goodhouse, M. G. Farquhar: J. Cell Biol. 103, 1235-1247 (1986)), the distribution of the two receptors differed: Tf-R remained the same as in controls, but M6P-R were localized in large vacuolated endosomes. To carry out double labeling experiments at the electron microscope level, transferrin gold **conjugates** (Tf-Au) were prepared, and **M6P** -R were detected by immunoperoxidase labeling. Tf-Au binding to the cell surface was specific as it was reduced approximately 70 to 79% in the presence of excess native Tf. When Clone 9 cells were incubated with Tf-Au at 37 degrees C for 5 to 30 min, or binding of Tf-Au was carried out at 4 degrees C followed by warming to 37 degrees C, Tf-Au was found within a peripheral tubulovesicular network and within multivesicular endosomes that were not labeled with anti-M6P-R. Other multivesicular endosomes of similar size and morphology were heavily labeled for M6P-R but contained little or no Tf-Au. Tf-Au and M6P-R were also found in separate endosomes in cells treated with NH4Cl. Native Tf was localized in the same compartments as Tf-Au by immunoperoxidase labeling of both Clone 9 cells and mouse myeloma cells. We conclude that in Clone 9 hepatocytes, Tf/Tf-R internalized from the cell surface and M6P-R bearing newly synthesized **lysosomal** enzymes from the Golgi deliver their ligands to two different subpopulations of multivesicular endosomes. The endosomal subpopulation visited by Tf/Tf-R is

known to correspond kinetically to early endosomes. The endosomal subpopulation heavily labeled for M6P-R presumably represent a later endosomal compartment which serves as the junction point where endocytosed ligands and newly synthesized **lysosomal** enzymes enroute to **lysosomes** meet.

CONTROLLED TERM: Ammonium Chloride: PD, pharmacology
Animals
Clone Cells
*Endocytosis
Fluorescent Antibody Technique
*Hexosephosphates: ME, metabolism
Immunoenzyme Techniques
Liver
Lysosomes: AN, analysis
Lysosomes: ME, metabolism
Lysosomes: UL, ultrastructure
*Mannosephosphates: ME, metabolism
Microscopy, Electron
*Organelles: AN, analysis
Organelles: ME, metabolism
Organelles: UL, ultrastructure
Rats
Receptor, IGF Type 2
Receptors, Cell Surface: AN, analysis
*Receptors, Cell Surface: ME, metabolism
Receptors, Transferrin: AN, analysis
*Receptors, Transferrin: ME, metabolism
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Transferrin: ME, metabolism

CAS REGISTRY NO.: 11096-37-0 (Transferrin); 12125-02-9 (Ammonium Chloride)
CHEMICAL NAME: 0 (Hexosephosphates); 0 (Mannosephosphates); 0 (Receptor, IGF Type 2); 0 (Receptors, Cell Surface); 0 (Receptors, Transferrin)

L74 ANSWER 29 OF 41 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 89002828 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2971437
TITLE: Preparation and application of a pentamannosyl monophosphate-bovine serum albumin conjugate.
AUTHOR: Baba T; Watanabe K; Yonezawa N; Hiroto M; Arai Y
CORPORATE SOURCE: Institute of Applied Biochemistry, University of Tsukuba, Ibaraki, Japan.
SOURCE: Carbohydrate research, (1988 Jun 15) 177 163-72.
Journal code: 0043535. ISSN: 0008-6215.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198811
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 20000303
Entered Medline: 19881115

ABSTRACT:
Pentamannosyl monophosphate, derived from Hansenula holstii O-phosphomannan, was conjugated to bovine serum albumin by reductive amination. The conjugate inhibited the binding of the porcine testis mannose 6-phosphate receptor to the insoluble phosphomannan core. A mannose 6-phosphate receptor with a molecular weight of 200,000 was purified from porcine liver membranes, using an affinity matrix of the conjugate attached to Sepharose 4B. Rabbits were immunised with

the conjugate, and the antisera were purified on a phosphomannan core-Sepharose 4B column in order to give an antibody which was specific for the 6-phosphate group and the equatorial HO-4 of D-mannose 6-phosphate. On Western blot analysis using the purified antibodies, ovalbumin, which contained a typical high-mannose type of oligosaccharide, was not recognised. However, a testicular glycoprotein fraction formed an immunostaining band. These results indicate the effectiveness of the **conjugate** as a ligand for ***mannose*** 6-**phosphate** receptors. The antibodies highly specific for mannose 6-phosphate may be used to detect or purify ***lysosomal*** enzymes.

CONTROLLED TERM: Check Tags: Male
Animals
*Antibodies: IP, isolation & purification
*Carrier Proteins: IP, isolation & purification
Carrier Proteins: ME, metabolism
Cell Membrane: ME, metabolism
Enzyme-Linked Immunosorbent Assay
*Hexosephosphates: CS, chemical synthesis
Liver: ME, metabolism
*Mannosephosphates: CS, chemical synthesis
Mannosephosphates: IM, immunology
Mannosephosphates: ME, metabolism
Molecular Weight
Receptor, IGF Type 2
*Serum Albumin, Bovine
*Serum Albumin, Bovine: CS, chemical synthesis
Swine
Testis: ME, metabolism

CAS REGISTRY NO.: 3672-15-9 (mannose-6-phosphate)

CHEMICAL NAME: 0 (Antibodies); 0 (Carrier Proteins); 0 (Hexosephosphates); 0 (Mannosephosphates); 0 (Receptor, IGF Type 2); 0 (Serum Albumin, Bovine); 0 (pentamannosyl phosphate substituted bovine serum albumin)

L74 ANSWER 30 OF 41 MEDLINE on STN DUPLICATE 17

ACCESSION NUMBER: 86168507 MEDLINE

DOCUMENT NUMBER: PubMed ID: 2870071

TITLE: Endocytosis of mannose-6-phosphate binding sites by mouse T-lymphoma cells.

AUTHOR: Bourguignon L Y; Balazovich K; Suchard S J; Hindsgaul O; Pierce M

CONTRACT NUMBER: AI19188 (NIAID)
CA35377 (NCI)
GM36353 (NIGMS)

SOURCE: Journal of cellular physiology, (1986 Apr) 127 (1) 146-61. Journal code: 0050222. ISSN: 0021-9541.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198605

ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 20000303
Entered Medline: 19860512

ABSTRACT:

The endocytosis and intracellular transport of **mannose**-6-***phosphate*** **conjugated** to bovine serum albumin (Man-6-P:BSA) by mouse T-lymphoma cells were investigated in detail using several methods of analysis, both morphological and biochemical. Man-6-P:BSA was labeled with fluorescein or 125I and used to locate both surface and intracellular Man-6-P

binding sites by light or electron microscopy, respectively. Incubation of cells with either fluorescent- or 125I-labeled Man-6-P:BSA at 0 degree C revealed a uniform distribution of the Man-6-P binding sites over the cell surface. Competition experiments indicate that the Man-6-P:BSA binding sites on the cell surface are the same receptors that can recognize **lysosomal** hydrolases. After as little as 1 min incubation at 37 degrees C, endocytosis of Man-6-P binding sites was clearly observed to occur through regions of the plasma membrane and via vesicles that also bound anticlathrin antibody. After a 5-15-min incubation of cells at 37 degrees C, the internalized ligand was detected first in the cis region of the Golgi apparatus and then in the Golgi stacks using both autoradiography and immunocytochemistry to visualize the ligand. The appearance of Man-6-P:BSA in the Golgi region after 15-30 min was confirmed by subcellular fractionation, which demonstrated an accumulation of Man-6-P:BSA in light membrane fractions that corresponded with the Golgi fractions. After a 30-min incubation at 37 degrees C, the internalized Man-6-P binding sites were localized primarily in **lysosomal** structures whose membrane but not lumen co-stained for acid phosphatase. These results demonstrate a temporal participation of clathrin-containing coated vesicles during the initial endocytosis of Man-6-P binding sites and that one step in the Man-6-P:BSA transport pathway between plasma membrane and the ***lysosomal*** structure can involve a transit through the Golgi stacks.

CONTROLLED TERM:
Animals
Autoradiography
Binding Sites
*Carrier Proteins: ME, metabolism
Cell Line
Cell Membrane: ME, metabolism
Clathrin: ME, metabolism
*Endocytosis
Endosomes: ME, metabolism
Golgi Apparatus: ME, metabolism
*Hexosephosphates: ME, metabolism
Lymphoma
Lysosomes: ME, metabolism
*Mannosephosphates: ME, metabolism
Mice
Microscopy, Electron
Receptor, IGF Type 2
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
T-Lymphocytes

CHEMICAL NAME: 0 (Carrier Proteins); 0 (Clathrin); 0 (Hexosephosphates); 0 (Mannosephosphates); 0 (Receptor, IGF Type 2)

L74 ANSWER 31 OF 41 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 86055862 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3905406
TITLE: Biosynthesis and intracellular transport of alpha-glucosidase and cathepsin D in normal and mutant human fibroblasts.
AUTHOR: Oude Elferink R P; Van Doorn-Van Wakeren J; Strijland A; Reuser A J; Tager J M
SOURCE: European journal of biochemistry / FEBS, (1985 Nov 15) 153 (1) 55-63.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198512

ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19851227

ABSTRACT:
In order to study the intracellular localization of the proteolytic processing steps in the maturation of alpha-glucosidase and cathepsin D in cultured human skin fibroblasts we have used incubation with glycyl-L-phenylalanine-beta-naphthylamide (Gly-Phe-NH-Nap) as described by Jadot et al. [Jadot, M., Colmant, C., Wattiaux-de Coninck, S. & Wattiaux, R. (1984) Biochem. J. 219,965-970] for the specific lysis of lysosomes. When a homogenate of fibroblasts was incubated for 20 min with 0.5 mM Gly-Phe-NH-Nap, a substrate for the lysosomal enzyme cathepsin C, the latency of the lysosomal enzymes alpha-glucosidase and beta-hexosaminidase decreased from 75% to 10% and their sedimentability from 75% to 20-30%. In contrast, treatment with Gly-Phe-NH-Nap had no significant effect on the latency of galactosyltransferase, a marker for the Golgi apparatus, and on the sedimentability of glutamate dehydrogenase and catalase, markers for mitochondria and peroxisomes, respectively. The maturation of alpha-glucosidase and cathepsin D in fibroblasts was studied by pulse-labelling with [35S]methionine, immunoprecipitation, polyacrylamide gel electrophoresis in the presence of sodium dodecyl sulphate and fluorography. When homogenates of labelled fibroblasts were incubated with Gly-Phe-NH-Nap prior to immunoprecipitation, 70-80% of all proteolytically processed forms of metabolically labelled alpha-glucosidase and cathepsin D was recovered in the supernatant. The earliest proteolytic processing steps in the maturation of alpha-glucosidase and cathepsin D appeared to be **coupled** to their transport to the **lysosomes.** Although both enzymes are transported via the **mannose-6-phosphate**-specific transport system, the velocity with which they arrived in the lysosomes was consistently different. Whereas newly synthesized cathepsin D was found in the lysosomes 1 h after synthesis, alpha-glucosidase was detected only after 2-4 h. When a pulse-chase experiment was carried out in the presence of 10 mM NH4Cl there was a complete inhibition of the transport of cathepsin D and a partial inhibition of that of alpha-glucosidase to the lysosomes. Leupeptin, an inhibitor of lysosomal thiol proteinases, had no effect on the transport of labelled alpha-glucosidase to the lysosomes. However, the early processing steps in which the 110-kDa precursor is converted to the 95-kDa intermediate form of the enzyme were delayed, a transient 105-kDa form was observed and the conversion of the 95-kDa intermediate form to the 76-kDa mature form of the enzyme was completely inhibited.(ABSTRACT TRUNCATED AT 400 WORDS)

CONTROLLED TERM:
Ammonium Chloride: PD, pharmacology
Biological Transport: DE, drug effects
*Cathepsin D: BI, biosynthesis
Cathepsin D: GE, genetics
Cathepsin D: ME, metabolism
Cell Line
Centrifugation, Density Gradient
Dipeptides: PD, pharmacology
Fibroblasts: EN, enzymology
*Glucosidases: BI, biosynthesis
Humans
Immunochemistry
Leupeptins: PD, pharmacology
Lysosomes: DE, drug effects
Lysosomes: EN, enzymology
Mutation
Organoids: DE, drug effects
Research Support, Non-U.S. Gov't
Skin
*alpha-Glucosidases: BI, biosynthesis
alpha-Glucosidases: GE, genetics

Searched by Barb O'Bryen, STIC 2-2518

alpha-Glucosidases: ME, metabolism
CAS REGISTRY NO.: 12125-02-9 (Ammonium Chloride); 21438-66-4 (glycylphenylalanine 2-naphthylamide); 24365-47-7 (leupeptin)
CHEMICAL NAME: 0 (Dipeptides); 0 (Leupeptins); EC 3.2.1.- (Glucosidases); EC 3.2.1.20 (alpha-Glucosidases); EC 3.4.23.5 (Cathepsin D)

L74 ANSWER 32 OF 41 MEDLINE on STN
ACCESSION NUMBER: 92126329 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1663372
TITLE: Molecular recognition and targeting of **lysosomal** proteins.
AUTHOR: von Figura K
CORPORATE SOURCE: Georg-August-Universitat, Gottingen, Germany.
SOURCE: Current opinion in cell biology, (1991 Aug) 3 (4) 642-6.
Ref: 23
Journal code: 8913428. ISSN: 0955-0674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 19920322
Last Updated on STN: 20000303
Entered Medline: 19920305

ABSTRACT:
Recent studies have established that in mammalian cells insulin-like growth factor-II can **couple** the large **mannose**-6-**phosphate** receptor to a GTP-binding protein and that the insulin-like growth factor-II-induced activation of the GTP-binding protein is inhibited by mannose-6-phosphate and **lysosomal** enzymes. In mouse, the gene for the large mannose-6-phosphate receptor is maternally imprinted.

CONTROLLED TERM:
Animals
Coated Pits, Cell-Membrane: ME, metabolism
Embryonic and Fetal Development
Enzymes: ME, metabolism
Enzymes: PD, pharmacology
Fungal Proteins: ME, metabolism
*GTP-Binding Proteins: ME, metabolism
Genes, Lethal
Humans
Insulin-Like Growth Factor II: AI, antagonists & inhibitors
*Insulin-Like Growth Factor II: PH, physiology
***Lysosomes: ME, metabolism**
Mammals: ME, metabolism
*Mannosephosphates: ME, metabolism
Mannosephosphates: PD, pharmacology
Membrane Proteins: ME, metabolism
Mice: EM, embryology
Mice: GE, genetics
Mucolipidoses: ME, metabolism
Phosphorylation
Phosphotransferases: ME, metabolism
Protein Binding
Protein Kinases: ME, metabolism
Protein Processing, Post-Translational
Receptor, IGF Type 2

Receptors, Cell Surface: GE, genetics
*Receptors, Cell Surface: ME, metabolism
*Signal Transduction
CAS REGISTRY NO.: 3672-15-9 (mannose-6-phosphate); 67763-97-7 (Insulin-Like Growth Factor II)
CHEMICAL NAME: 0 (Enzymes); 0 (Fungal Proteins); 0 (Mannosephosphates); 0 (Membrane Proteins); 0 (Receptor, IGF Type 2); 0 (Receptors, Cell Surface); EC 2.7 (Phosphotransferases); EC 2.7.1.37 (Protein Kinases); EC 3.6.1.- (GTP-Binding Proteins)
GENE NAME: MPR300; VPS15

L74 ANSWER 33 OF 41 AGRICOLA Compiled and distributed by the National Agricultural Library of the Department of Agriculture of the United States of America. It contains copyrighted materials. All rights reserved. (2005) on STN DUPLICATE 9

ACCESSION NUMBER: 95:67786 AGRICOLA
DOCUMENT NUMBER: IND20487416
TITLE: Cloning and expression of the cDNA of chicken cation-independent mannose-6-phosphate receptor.
AUTHOR(S): Zhou, M.; Ma, Z.; Sly, W.S.
CORPORATE SOURCE: St. Louis University School of Medicine, St. Louis, MO.
AVAILABILITY: DNAL (500 N21P)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, Oct 10, 1995. Vol. 92, No. 21. p. 9762-9766
Publisher: Washington, D.C. : National Academy of Sciences,
CODEN: PNASA6; ISSN: 0027-8424
NOTE: Includes references
PUB. COUNTRY: District of Columbia; United States
DOCUMENT TYPE: Article; Conference
FILE SEGMENT: U.S. Imprints not USDA, Experiment or Extension
LANGUAGE: English
ABSTRACT:
We cloned and sequenced the 8767-bp full-length cDNA for the chicken cation-independent mannose-6-phosphate receptor (CI-MPR), of interest because, unlike its mammalian homologs, it does not bind insulin-like growth factor II (IGF-II). The cDNA encodes a protein of 2470 aa that includes a putative signal sequence, an extracytoplasmic domain consisting of 15 homologous repeat sequences, a 23-residue transmembrane sequence, and a 161-residue cytoplasmic sequence. Overall, it shows 60% sequence identity with human and bovine CI-MPR homologs, and all but two of 122 cysteine residues are conserved. However, it shows much less homology in the N-terminal signal sequence, in repeat 11, which is proposed to contain the IGF-II-binding site in mammalian CI-MPR homologs, and in the 14-aa residue segment in the cytoplasmic sequence that has been proposed to mediate G-protein-**coupled** signal transduction in response to IGF-II binding by the human CI-MPR. Transient expression in COS-7 cells produced a functional CI-MPR which exhibited mannose-6-phosphate-inhibitable binding and mediated endocytosis of recombinant human beta-glucuronidase. Expression of the functional chicken CI-MPR in mice lacking the mammalian CI-MPR should clarify the controversy over the physiological role of the IGF-II-binding site in mammalian CI-MPR homologs.

CLASSIFICATION: L200 Animal Breeding and Genetics
CONTROLLED TERM (CABA): amino acid sequences; binding proteins; cell lines; chickens; complementary dna; exons; gene expression; gene transfer; introns; mannose; mice; nucleotide sequences; receptors; sugar phosphates

SUPPLEMENTARY TERM: GenBank U35037; molecular sequence data
CAS REGISTRY NO.: **3672-15-9** (MANNOSE 6-PHOSPHATE)
9001-45-0 (B-GLUCURONIDASE)
169717-04-8 (GENBANK U35037)
52-90-4Q, 62488-11-3Q (CYSTEINE)
3458-28-4Q, 31103-86-3Q (MANNOSE)

L74 ANSWER 34 OF 41 on STN PASCAL COPYRIGHT 2005 INIST-CNRS. ALL RIGHTS RESERVED.
ACCESSION NUMBER: 2003-0150755 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2003 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Glycosyl transferases and glycosidases of glycoprotein biosynthesis with emphasis on Candida albicans and Entamoeba histolytica
Recent research developments in microbiology. Vol. 4 (2000) ; Part II
AUTHOR: LOPEZ-ROMERO Everardo; FLORES-CARREON Arturo; ARROYO-FLORES Blanca L.; TORRE-BOUSCOULET Ma. Eugenic; BRAVO-TORRES Jose C.; VILLAGOMEZ-CASTRO Julio C.; BALCAZAR-OROZCO Rosalia
PANDALAI S. G.
CORPORATE SOURCE: Departamento de Genetica y Biologia Molecular, CINVESTAV del IPN, Apartado Postal No. 14-740, 07000 Mexico, D.F., Mexico; Instituto de Investigacion en Biologia Experimental, Facultad de Quimica, Universidad de Guanajuato, Apartado Postal No. 187, Guanajuato, Gto. 36000, Mexico
SOURCE: Recent research developments in microbiology, (2000), 667-681, 117 refs.
ISBN: 81-7736-014-0
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: India
LANGUAGE: English
AVAILABILITY: INIST-L 28294, 354000108086660160
ABSTRACT: We have investigated the presence and biochemical properties of glycosyl transferases and glycosidases involved in glycoprotein biosynthesis in two human pathogens: the fungus Candida albicans and the parasite protozoan Entamoeba histolytica. These include dolichol phosphate mannose synthase (DPMS), dolichol phosphate glucose synthase (DPGS), protein mannosyl transferases (PMT), N-acetylglucosaminyl-1-P transferase (GPT) and N-acetylglucosaminyl transferase (GT) and the processing glycosydases α-glucosidases and α-mannosidases. In C. albicans, we optimized conditions to determine activity of DPMS and the functionally-**coupled** PMT in a mixed membrane fraction. Solubilization with Nonidet P-40 rendered an **enzyme** fraction that channeled over 80 % of the total transferred radioactivity into dolichol **phosphate mannose** (Dol-P-Man) whereas only a minor fraction of protein was labeled. Most PMT activity remained particulate. DPGS was also studied in both membranes and a NP-40-solubilized fraction from yeast cells of C. albicans. On the other hand, a membrane fraction from E. histolytica showed the ability to incorporate over 80 % of labeled mannose from GDP-Man

into different lipid sugar products with Dol-P-Man representing about 25 % of the total transferred radioactivity. The development of a protocol to obtain a soluble fraction that transferred the sugar selectively to Dol-P-Man allowed us to partially purify the the enzyme. Among other properties, we investigated the reversion of the mannosyl transfer reaction and the regulation of amoeba DPMS by enzyme phosphorylation. Enzymes catalyzing the early steps of the N-linked glycosylation pathway, i.e., GPT and GT, cosolubilized with DPMS and were also characterized. With respect to processing glycosidases, analysis of subcellular distribution of a-glucosidase in C. albicans and E. histolytica demonstrated that most of enzyme activity in both organisms is in soluble form. Major properties of this enzyme in crude and partially purified fractions were investigated to determine their potential role in N-glycan processing. Purification of α-mannosidase activity from C. albicans, which was also found as a soluble enzyme, allowed us to separate two isoforms, E-I and E-II, whose role in processing of N-linked oligosaccharides is discussed.

CLASSIFICATION CODE: 002A05D04; Life sciences; Biological sciences; Microbiology; Mycology
002A11C; Life sciences; Biological sciences

L74 ANSWER 35 OF 41 PASCAL COPYRIGHT 2005 INIST-CNRS. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1998-0472765 PASCAL

TITLE (IN ENGLISH): CATHEPSIN D INHIBITORS : Synthesis and biological evaluation of pepstatin A associated with phosphomannosyles

TITLE (IN FRENCH): INHIBITEURS DE LA CATHEPSINE D : Synthese et evaluation biologique de phosphomannosyles associes a la pepstatine

AUTHOR: HAMDAOUI Bassou; MONTERO Jean Louis (dir.)

CORPORATE SOURCE: Universite de Montpellier 2, Montpellier, France (tutelle)

SOURCE: (1993-01), 150 refs.
145 p.
Dissertation Information: Universite de Montpellier 2. Montpellier. FRA, Th. doct., 93MON20003

DOCUMENT TYPE: Dissertation

BIBLIOGRAPHIC LEVEL: Monographic

COUNTRY: France

LANGUAGE: French

SUMMARY LANGUAGE: French; English

AVAILABILITY: INIST-T 119375, T93MON20003 0000

ABSTRACT (IN FRENCH): La Cathepsine D est une protease **lysosomale** dont la surproduction est liee a l'apparition de metastases dans le cancer du sein. Au cours de ce travail nous avons decrit la synthese et l'evaluation biologique de composes bifonctionnels susceptibles d'inhiber la Cathepsine D. D'autre part nous avons prepare une neoglycoproteine utilisee comme ligand du recepteur mannose-6-phosphate. Ces composes comportent d'une part le groupement mannose-6-phosphate

permettant leur penetration cellulaire par l'intermediaire des recepteurs membranaires et d'autre part la pepstatine puissant inhibiteur de la Cathepsine D. Le **couplage** de la pepstatine a un **mannose**-6-**phosphate** a ete realise par amination de la position anomerique du sucre par la pepstatine preassociee au 1,3-diaminopropane utilise comme bras de jonction. La pepstatine **couplee** a deux entites . **mannose**-6-**phosphate** a ete preparee reaction de thiocarbamoylation de la diamine peptide (derivee de la pepstatine) par l'isothiocyanate de phenyloxy-mannose-6-phosphate. Ce dernier a ete prepare a partir du p-nitrophenyl-D-mannopy rannose par phosphorylation selective en 6, suivie d'une reduction en amine et transformation de celle-ci en isothiocyanate. La serum albumine bovine (BSA) portant une trentaine de groupements mannose-6-phosphate a ete preparee par traitement de la BSA en milieu alcalin par l'isothiocyanate de phenyloxymannose-6-phosphate. Les produits synthetises ont presente des resultats biologiques significatifs. La pepstatine **couplee** a deux entites **mannose**-6-**phosphate** inhibe la proliferation et le pouvoir invasif des cellules cancereuses. La neoglycoproteine inhibe significativement la migration des cellules metastatiques a travers la membrane basale reconstituee.

CLASSIFICATION CODE: 002B02R01; Life sciences; Medical sciences; Pharmacology; Oncology

CONTROLLED TERM: Cathepsin D; Enzyme inhibitor; Antimetastatic agent; Antineoplastic agent; Chemical synthesis; Biological activity; In vitro; Pepstatin; Amination

BROADER TERM: Aspartic endopeptidases; Peptidases; Hydrolases; Enzyme

L74 ANSWER 36 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:205507 BIOSIS

DOCUMENT NUMBER: PREV200400206023

TITLE: The single transmembrane IGF - II/**M6P** receptor **couples** to a G - protein and regulates central cholinergic function in the rat brain.

AUTHOR(S): Hawkes, C. [Reprint Author]; Harris, K.; Fu, W.; Jhamandas, J.; Kar, S. [Reprint Author]

CORPORATE SOURCE: Dept. Neurol. and Neurosci, McGill Univ, Montreal, PQ, Canada

SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 896.10. http://sfn.scholarone.com. e-file.
Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 14 Apr 2004
Last Updated on STN: 14 Apr 2004

ABSTRACT:The insulin-like growth factor-II/mannose-6-phosphate (IGF-II/M6P) receptor is a single pass transmembrane glycoprotein which functions in the

intracellular trafficking of **lysosomal** enzymes, and in the activation/degradation of extracellular IGF-II and M6P-containing ligands. Evidence from in vitro non-neuronal systems has indicated that the IGF-II/M6P receptor can also mediate IGF-II signaling under certain circumstances. We have found that the receptor is widely distributed in the adult rat CNS, and colocalizes with cholinergic neurons. We have shown that Leu27IGF-II, an IGF-II analog, competes for (125I)IGF-II binding in the adult rat hippocampus more potently than for (125I)IGF-I and (125I)Insulin binding sites. Our pharmacological and immunoprecipitation data support a direct interaction of the IGF-II/M6P receptor with an inhibitory G-protein. Whole cell currents recorded from acutely dissociated rat basal forebrain neurons were reduced upon application of Leu27IGF-II(50 nM) and this reduction was not apparent in neurons pre-incubated with pertussis toxin. Additionally, Leu27IGF-II, acting via the IGF-II/M6P receptor, dose-and time-dependently potentiated endogenous acetylcholine (ACh) release from the rat hippocampus and striatum. Furthermore, application of Leu27IGF-II resulted in an increase in the excitability of rat basal forebrain neurons. Leu27IGF-II-stimulated ACh release does not involve alterations in HACU or ChAT activity, but does induce phosphorylation and translocation of phospho-PKCalpha, GAP-43 and MARCKS. Thus, we provide the first direct evidence that i) the single transmembrane IGF-II/**M6P** receptor **couples** to a G-protein and ii) the receptor can modulate cholinergic function via G-protein and PKC activation.

CONCEPT CODE:
General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Enzymes - General and comparative studies: coenzymes 10802
Endocrine - General 17002
Nervous system - Physiology and biochemistry 20504

INDEX TERMS:
Major Concepts
Nervous System (Neural Coordination)

INDEX TERMS:
Parts, Structures, & Systems of Organisms
CNS: nervous system; basal forebrain neurons: nervous system; brain: nervous system; cholinergic neurons: nervous system; hippocampus: nervous system; neurons: nervous system

INDEX TERMS:
Chemicals & Biochemicals
ChAT; G-proteins; GAP-43; IGF-II [insulin-like growth factor-II]; IGF-II/M6P receptor; MARCKS; PKC; PKC-alpha; acetylcholine; glycoprotein; **lysosomal** enzymes; mannose-6-phosphate; pertussis toxin

INDEX TERMS:
Methods & Equipment
immunoprecipitation: immunologic techniques, laboratory techniques

INDEX TERMS:
Miscellaneous Descriptors
cholinergic function

ORGANISM:
Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat (common): adult
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER:
67763-97-7 (IGF-II)

Searched by Barb O'Bryen, STIC 2-2518

67763-97-7 (insulin-like growth factor-II)
51-84-3 (acetylcholine)
3672-15-9 (mannose-6-phosphate)

L74 ANSWER 37 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1985:249153 BIOSIS
DOCUMENT NUMBER: PREV198579029149; BA79:29149
TITLE: PROTEIN BODIES AND VACUOLES AS LYSOSOMES INVESTIGATIONS INTO THE ROLE OF **MANNOSE**-6-**PHOSPHATE** IN INTRACELLULAR TRANSPORT OF GLYCOSIDASES IN PEA PISUM-SATIVUM CULTIVAR BURPEEANA COTYLEDONS.
AUTHOR(S): GAUDREAUALT P-R [Reprint author]; BEEVERS L
CORPORATE SOURCE: DEP BOTANY MICROBIOL, UNIV OKLA, NORMAN, OKLA 73019, USA
SOURCE: Plant Physiology (Rockville), (1984) Vol. 76, No. 1, pp. 228-232.
CODEN: PLPHAY. ISSN: 0032-0889.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ABSTRACT:**Mannose**-6-**phosphate** was not found in the oligosaccharide moiety of glycoproteins from pea (P. sativum L. cv. Burpeeana) cotyledons using an assay system sensitive to 10 pmol of **mannose**-6-***phosphate.*** Retention of glycosidase activity from pea seedlings and pea cotyledons was not observed on Sepharose-**coupled** phosphomannosyl receptor proteins isolated from bovine liver which were, however, able to retain phosphomannosylated hexosaminidase purified from Dictyostelium discoideum secretions. Although Sepharose-**coupled** phosphomannosylated **hexosaminidase** from Dictyostelium was able to bind phosphomannosyl receptors from bovine liver, it was not possible to detect the retention of any protein from acetone powder extracts of pea seedlings or from endoplasmic reticulum-associated proteins of pea cotyledons. ***Mannose*** -6-**phosphate** apparently does not play a role in the targeting of hydrolytic enzymes from the endoplasmic reticulum to the protein bodies in pea cotyledons.
CONCEPT CODE: Cytology - Plant 02504
Biochemistry methods - Proteins, peptides and amino acids 10054
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Minerals 10069
Enzymes - Physiological studies 10808
Movement 12100
Digestive system - General and methods 14001
Morphology, anatomy and embryology of plants 51000
Plant physiology - Enzymes 51518
Plant physiology - Translocation, accumulation 51520
Horticulture - Vegetables 53008
Invertebrata: comparative, experimental morphology, physiology and pathology - Protozoa 64002
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Horticulture (Agriculture); Physiology
INDEX TERMS: Miscellaneous Descriptors
DICTYOSTELIUM-DISCOIDEUM BOVINE LIVER PHOSPHOMANNOSYL RECEPTOR HYDROLYTIC ENZYMES HEXOSAMINIDASE
ORGANISM: Classifier
Myxophyta 15700

Searched by Barb O'Bryen, STIC 2-2518

Super Taxa
Fungi; Plantae
Taxa Notes
Fungi, Microorganisms, Nonvascular Plants, Plants
ORGANISM: Classifier
Leguminosae 26260
Super Taxa
Dicotyledones; Angiospermae; Spermatophyta; Plantae
Taxa Notes
Angiosperms, Dicots, Plants, Spermatophytes, Vascular Plants
ORGANISM: Classifier
Sarcodina 35300
Super Taxa
Protozoa; Invertebrata; Animalia
Taxa Notes
Animals, Invertebrates, Microorganisms, Protozoans
ORGANISM: Classifier
Bovidae 85715
Super Taxa
Artiodactyla; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates
REGISTRY NUMBER: **3672-15-9** (**MANNOSE**-6-**PHOSPHATE**
)
9032-92-2D (GLYCOSIDASES)
9012-33-3 (HEXOSAMINIDASE)
9027-52-5 (HEXOSAMINIDASE)

L74 ANSWER 38 OF 41 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 1989-00987 BIOTECHDS
TITLE: Hydrolysis products of Pichia (Hansenula) holstii O-phosphonomannan and uses in phosphomannosyl receptor characterization;
Pichia holstii phosphono-mannan preparation (conference paper)
AUTHOR: Slodki M E
LOCATION: Northern Regional Research Center, Agricultural Research Service, U.S. Department of Agriculture, Peoria, Illinois 61604, USA.
SOURCE: Prog.Biotechnol.; (1987) 3, 109-19
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT: The diploid yeast strain Pichia holstii NRRL Y-2448 (Hansenula holstii) produced extracellular O-phosphono-alpha-D-mannan when grown in aerated, submerged batch culture on D-glucose (50 g/l) and excess orthophosphate. In shake flasks, over 60% conversion of the sugar to product was obtained in 3 days. Mannan was recovered by precipitation with 1 volume of a lower alcohol in the presence of KCl. Mild acid hydrolysis of the O-phosphonomannan liberated a pentasaccharide monophosphate (90%) and a high mol.weight monoester (10%). Both products were used to study mammal **mannose**-6-**phosphate** receptors. The pentasaccharide monophosphate was **coupled** to proteins in order to target them to **lysosomal** receptors. There was greater interest in the high-mol.weight fragment. It was a potent inhibitor of mannose phosphate binding to membrane receptors and was used as an affinity

ligand for isolation of such receptors. Methylation analysis indicated a highly branched structure that consisted of a 1,6-linked backbone chain to which 1,2- and 1,3-linked side chains were attached at C2 positions. Nonreducing end groups were likely sites of phosphorylation. (35 ref)

CLASSIFICATION: H OTHER CHEMICALS; H1 Polymers; A MICROBIOLOGY; A2 Fermentation; C CHEMISTRY; C1 Analysis and Structure

CONTROLLED TERMS: PICHIA HOLSTII PHOSPHONO-MANNAN PREP., APPL. RECEPTOR CHARACTERIZATION YEAST FUNGUS POLYSACCHARIDE

L74 ANSWER 39 OF 41 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 86045329 EMBASE
DOCUMENT NUMBER: 1986045329
TITLE: Biosynthesis and intracellular transport of α-glucosidase and cathepsin D in normal and mutant human fibroblasts.
AUTHOR: Oude Elferink R.P.J.; Van Doorn-Van Wakeren J.; Strijland A.; et al.
CORPORATE SOURCE: Laboratory of Biochemistry, University of Amsterdam, NL-1000 HD Amsterdam, Netherlands
SOURCE: European Journal of Biochemistry, (1985) Vol. 153, No. 1, pp. 55-63.
CODEN: EJBCAI
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 911210
Last Updated on STN: 911210

ABSTRACT: In order to study the intracellular localization of the proteolytic processing steps in the maturation of α-glucosidase and cathepsin D in cultured human skin fibroblasts we have used incubation with glycyl-L-phenylalanine-β-naphthylamide (Gly-Phe-NH-Nap) as described by Jadot et al. [Jadot, M., Colmant, C., Wattiaux-de Coninck, S. & Wattiaux, R. (1984) Biochem. J. 219, 965-970] for the specific lysis of lysosomes. When a homogenate of fibroblasts was incubated for 20 min with 0.5 mM Gly-Phe-NH-Nap, a substrate for the lysosomal enzyme cathepsin C, the latency of the lysosomal enzymes α-glucosidase and β-hexosaminidase decreased from 75% to 10% and their sedimentability from 75% to 20-30%. In contrast, treatment with Gly-Phe-NH-Nap had no significant effect on the latency of galactosyltransferase, a marker for the Golgi apparatus, and on the sedimentability of glutamate dehydrogenase and catalase, markers for mitochondria and peroxisomes, respectively. The maturation of α-glucosidase and cathepsin D in fibroblasts was studied by pulse-labelling with [35S]methionine, immunoprecipitation, polyacrylamide gel electrophoresis in the presence of sodium dodecyl sulphate and fluorography. When homogenates of labelled fibroblasts were incubated with Gly-Phe-NH-Nap prior to immunoprecipitation, 70-80% of all proteolytically processed forms of metabolically labelled α-glucosidase and cathepsin D was recovered in the supernatant. The earliest proteolytic processing steps in the maturation of α-glucosidase and cathepsin D appeared to be **coupled** to their transport to the **lysosomes.** Although both enzymes are transported via the **mannose**-6-**phosphate**-specific transport system, the velocity with which they arrived in the lysosomes was consistently different. Whereas newly synthesized cathepsin D was found in the lysosomes 1 h after synthesis, α-glucosidase was detected only after 2-4 h. When a pulse-chase experiment was carried out in the presence of 10 mM NH_4Cl there was a complete inhibition of the transport of cathepsin D and a partial inhibition of that of α-glucosidase to the lysosomes. Leupeptin, an inhibitor of

lysosomal thiol proteinases, had no effect on the transport of labelled α-glucosidase to the lysosomes. However, the early processing steps in which the 110-kDa precursor is converted to the 95-kDa intermediate form of the enzyme were delayed, a transient 105-kDa form was observed and the conversion of the 95-kDa intermediate form to the 76-kDa mature form of the enzyme was completely inhibited. Two cell lines from patients with glycogenosis type II have been described in which newly synthesized α-glucosidase is not phosphorylated [Reuser, A.J.J., Kroos, M., Oude Elferink, R.P.J. & Tager, J.M. (1985) J. Biol. Chemical 260, 8336-8341]; in these specific cell lines newly synthesized α-glucosidase is not transported to the lysosomes but is rapidly degraded in a prelysosomal compartment. In a third glycogenosis type II cell line, in which phosphorylation of α-glucosidase is normal yet no proteolytic processing occurs (loc. cit.), there is no transport of the enzyme to the lysosomes.

CONTROLLED TERM: Medical Descriptors:
*glycogen storage disease type 2
fibroblast
priority journal
human
etiology
human cell
Drug Descriptors:
*alpha glucosidase
*cathepsin d
CAS REGISTRY NO.: (alpha glucosidase) 9001-42-7; (cathepsin d) 9025-26-7

L74 ANSWER 40 OF 41 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-339533 [29] WPIDS
DOC. NO. CPI: C2000-103003
TITLE: New compounds with drug carriers, which specifically accumulate in hepatic stellate cells, useful as active targeting ingredients in compositions for therapy, prophylaxis or diagnosis of diseases, e.g. fibrosis, inflammation or tumors.
DERWENT CLASS: B04
INVENTOR(S): BELJAARS, E; MEIJER, D K F; POELSTRA, K; SCHUPPAN, D B I
PATENT ASSIGNEE(S): (UYGR-N) RIJKSUNIV GRONINGEN; (TEWE-N) STICHTING TECH WETENSCHAPPEN; (UYGR-N) RIJKSUNIVERSITEIT TE GRONINGEN
COUNTRY COUNT: 84
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2000023113	A1	20000427	(200029)*	EN	38	A61K047-48
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW						
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW						
AU 9895609	A	20000508	(200037)			A61K047-48
EP 1117443	A1	20010725	(200143)	EN		A61K047-48
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI						
JP 2002532384	W	20021002	(200279)		45	A61K047-48
AU 770340	B2	20040219	(200454)#			A61K047-48
US 6844319	B1	20050118	(200506)			A61K038-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000023113	A1	WO 1998-NL579	19981008
AU 9895609	A	AU 1998-95609	19981008
		WO 1998-NL579	19981008
EP 1117443	A1	EP 1998-949252	19981008
		WO 1998-NL579	19981008
JP 2002532384	W	WO 1998-NL579	19981008
		JP 2000-576886	19981008
AU 770340	B2	AU 1998-95609	19981008
US 6844319	B1	WO 1998-NL579	19981008
		US 2001-806837	20010723

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9895609	A	Based on	WO 2000023113
EP 1117443	A1	Based on	WO 2000023113
JP 2002532384	W	Based on	WO 2000023113
AU 770340	B2	Previous Publ.	AU 9895609
		Based on	WO 2000023113
US 6844319	B1	Based on	WO 2000023113

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INT. PATENT CLASSIF.:
MAIN: A61K038-00; A61K047-48
SECONDARY: A61K009-00; A61K047-42; A61P001-00; A61P007-00; A61P009-10; A61P011-00; A61P013-00; A61P019-02; A61P029-00; A61P043-00; C07K011-02; C07K014-71; C07K014-715; C07K014-765; C07K019-00; C12Q001-02; G01N033-566
ADDITIONAL: G01N033-15

BASIC ABSTRACT:

WO 200023113 A UPAB: 20000617

NOVELTY - A compound (I), comprising a carrier molecule linked to at least one cyclic peptide comprising at least one sequence encoding a cell receptor recognizing peptide (RRP), is new. (I) is not a naturally occurring receptor agonist or antagonist.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a compound (II) capable of recognizing and binding a mannose 6 phosphate receptor, comprising a carrier molecule linked to a second molecule capable of recognizing and binding mannose 6 phosphate receptor occupying at least 20% of the carrier molecule linking sites. (II) is not latent tumor growth factor beta, thyroglobulin or a **lysosomal** protein.

ACTIVITY - Antiinflammatory; antifibrotic; antiarteriosclerotic; cytostatic; antirheumatic; antiarthritic; antiulcer; nephrotropic; antibacterial; immunosuppressive.

Pyrrolidine-dithiocarbamate (PDTC, which is an inhibitor of the transcription factor NF-kappaB) was attached to M6P28-HSA (**mannose -6-phosphate** - human serum albumin) by **coupling** the carboxylic groups of PDTC to lysine groups of HSA. This compound was administered to rats with liver fibrosis induced by bile duct ligation. Rats receiving the conjugate 1, 3 and 5 days after the bile duct ligation displayed less proliferation of HSC in the parenchymal area at day 7 as compared to rats receiving no treatment or PDTC alone after induction of fibrosis.

MECHANISM OF ACTION - Platelet derived growth factor receptor antagonist; collagen type VI receptor antagonist; transforming growth

factor beta receptor antagonist; tumor necrosis factor alpha receptor agonist.

USE - (I) and (II) are useful as active targeting ingredients for manufacturing a pharmaceutical composition for the therapy, prophylaxis or diagnosis of a fibrotic disease, sclerotic disease and chronic or acute inflammatory processes. Inflammatory processes may include glomerulosclerosis, interstitial fibrosis, lung fibrosis, atherosclerosis, rheumatoid arthritis, Crohn's disease, colitis ulcerosa, glomerulonephritis and sepsis. (I) and (II) are also useful as active targeting ingredients for manufacturing a pharmaceutical composition for the therapy, prophylaxis or diagnosis of a disease related to proliferation of HSC (Hepatic Stellate Cells). The compound (II) is also useful for the therapy, prophylaxis or diagnosis of conditions such as cell proliferation associated pathology, including tumors, or fibroblast, endothelial, or osteoblast proliferation associated pathology (all claimed).

Dwg.0/10

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B04-H20A; B04-K01; B04-K01G; B04-K01J; B04-K01K; B04-L01; B04-N04B; B11-C08E; B12-K04A; B12-K04A1; B14-A01; B14-C03; B14-C09B; B14-E08; B14-F07; B14-G02; B14-H01B; B14-N10

L74 ANSWER 41 OF 41 ANABSTR COPYRIGHT 2005 RSC on STN
AN 65(18):F135 ANABSTR
TI Mannose 6-phosphate quantitation in glycoproteins using high-pH anion-exchange chromatography with pulsed amperometric detection.
AU Zhou, Q.; Kyazike, J.; Edmunds, T.; Higgins, E. (Structural Protein Chem., Genzyme Corp., Framingham, MA 01701, USA)
SO Anal. Biochem. (2002) 306(2), 163-170
CODEN: ANBCA2 ISSN: 0003-2697
DT Journal
LA English
AB The method involves the hydrolysis of glycoproteins with 6.75M-trifluoroacetic acid followed by the determination of the released mannose 6-phosphate by high-pH anion-exchange chromatography **coupled** with pulsed amperometric detection. **Mannose** 6-**phosphate** was separated on a CarboPac PA10 column (25 cm + 4 mm i.d.) with a gradient elution programme involving the use of 100mM-NaOH and 100mM-NaOH-1M-sodium acetate as eluents, at a total flow rate of 1 ml/min. The method was applied in the determination of mannose 6-phosphate in a recombinant **lysosomal** enzyme, human α-galactoside A. The amount of mannose 6-phosphate was linearly related to the amount of α-galactoside A hydrolyzed and was sensitive to as little as 2.5 μg of α-galactoside A, which contains 117 pmol of mannose 6-phosphate, and the response was linear up to 40 μg of α-galactoside A. The method could also be used to determine mannose 6-phosphate in electroblots following the hydrolysis reaction.
CC *F Clinical and Biochemical Analysis (50000)
B Chromatography and Electrophoresis
IT Analyte(s):
3672-15-9, mannose 6-phosphate
(quantitation of, in glycoproteins, by ion-exchange chromatography, detectors for, amperometric)
Matrix:
glycoproteins

(quantitation of mannose 6-phosphate in, by ion-exchange chromatography, detectors for, amperometric)
Concepts:
chromatography, ion-exchange
(detectors for, amperometric, in quantitation of mannose 6-phosphate, in glycoproteins)

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